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L3: Entry 19 of 21 File: DWPI Oct 28, 1987

DERWENT-ACC-NO: 1987-329624
DERWENT-WEEK: 198747

TITLE: Improved daily yield of colostrum - by addn. of medicinal herbs as Galega officinalis to fodder

INVENTOR: NAGY, L

PATENT-ASSIGNEE:

ASSIGNEE	CODE
JANOVSZKI J	JANOI

PRIORITY-DATA: 1986HU-0001033 (March 12, 1986)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
HU 43248 T	October 28, 1987		000	

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
HU 43248T	March 12, 1986	1986HU-0001033	

INT-CL (IPC): A23K 1/00

ABSTRACTED-PUB-NO: HU 43248T
BASIC-ABSTRACT:

Medicinal herbs in fodder improve daily yield of colostrum. (All pts.wt.); 8.5-25 oat grains (Avena futua), 10-35 barley (Hordeum vulgare), 15-42 maize (Zea Mays) 2-10 stem, leaves and flowers of lucerne (Medicag Sativa), stem and leaves of 65-25 goats rue (Galega efficinalis, or medicinal extract of these prepd. by known methods, a liq. or solid concentrate, a liophylizate, a flour or bran based focloles or a pill prepd. from them.

T ITLE-TERMS: IMPROVE DAILY YIELD COLOSTRUM ADD MEDICINE HERB OFFICINALIS FODDER

DERWENT-CLASS: B04 C03 D13

CPI-CODES: B04-A07D2; B04-A07D4; B04-A07D5; B12-L09; B12-M11D; C04-A07D2; C04-A07D4; C04-A07D5; C12-L09; C12-M11D; D03-G04;

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1987-140487

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File 440:Current Contents Search(R) 1990-2003/Aug 07
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*File 113: This file is closed (no updates)

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-key terms

Set Items Description
S1 331 (ENTEROBACTER? OR ENTERO(W)BACTER? OR (KLEBSIEL? OR K)(W)P-NEUMON?) AND (OMPA OR (OMP OR OUTER(W)MEMBRAN?(W)PROTEIN)(W)A)
S2 6 KPOMPA OR KP(W)(OMPA OR (OMP OR OUTER(W)MEMBRAN?(W)PROTEIN-)(W)A)
S3 51 (S1 OR S2) AND (ANTIGEN(1W)CELL? ? OR DENDRIT?? OR MONOCYT-?? OR B(W)(CELL? ? OR LYMPHOCYTE? ?) OR DC(20N)DENDRIT??)
S4 33 RD (unique items)
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4/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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16109857 PASCAL No.: 03-0268340
*Outer"** *membrane"** *protein"** *A"** (*OmpA"**): a new pathogen-associated molecular pattern that interacts with *antigen"** presenting *cells"**: impact on vaccine strategies
Therapeutic vaccines against HIV and cancers, 23-26 June 2002, Les Pensieres, Veyrier-du-Lac, Annecy, France
JEANNIN Pascale; MAGISTRELLI Giovanni; GOETSCH Liliane; HAEUW Jean-Francois; THIEBLEMONT Nathalie; BONNEFOY Jean-Yves; DELNESTE Yves
AUTRAN Brigitte, ed; FRIDMAN Herve, ed; LOTZE Michael, ed; WALKER Bruce, ed
Centre d'Immunologie Pierre Fabre, 5, Avenue Napoleon III, 74164 Saint-Julien en Genevois, France; CNRS-UMR 8603, Necker Hospital, 161 rue de Sevres, 75743 Paris, France
Merieux Foundation, 69227 Lyon, France
Therapeutic vaccines against HIV and cancers (Veyrier-du-Lac (Annecy) FRA) 2002-06-23
Journal: Vaccine. Supplement, 2002, 20 (PART4) A23-A27

Searcher : Shears 308-4994

Language: English
*Outer"** *membrane"** *protein"** *A"** (*OmpA"**) is a class of proteins highly conserved among the *Enterobacteriaceae"** family and throughout evolution. We have observed that *antigen"** presenting *cells"** (APCs) recognize and are activated by the recombinant *OmpA"** from *Klebsiella"** *pneumoniae"** (*KpOmpA"**). *KpOmpA"** triggers cytokine production by macrophages and *dendritic"** cells (*DC"**), induces *DC"** maturation and signals via Toll-like receptor 2. *KpOmpA"** also interacts with endocytic receptor(s) expressed on DC and macrophages. Tumor antigens coupled to *KpOmpA"** are taken up by APCs and gain access to the MHC class I pathway, triggering the initiation of protective anti-tumor cytotoxic responses in the absence of CD4 T cell help and adjuvant. Thus, *OmpA"** appears as a new type of pathogen-associated molecular pattern (PAMP) usable as a vector in anti-infectious and therapeutic anti-tumor vaccines to elicit CTLs.

4/3,AB/2 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

15772534 PASCAL No.: 02-0485817
Streptococcus pneumoniae polysaccharides conjugated to the *outer"** *membrane"** *protein"** *A"** from *Klebsiella"** *pneumoniae"** elicit protective antibodies
LIBON Christine; HAEUW Jean Francois; CROUZET Francoise; MUGNIER Chantal; BONNEFOY Jean Yves; BECK Alain; CORVAIA Nathalie
Centre d'Immunologie Pierre Fabre, 5 Avenue Napoleon III, 74164 St. Julien en Genevois, France
Journal: Vaccine, 2002, 20 (17-18) 2174-2180
Language: English
Polysaccharides (PSs) derived from Streptococcus pneumoniae include more than 90 serotypes and differ greatly in their immunogenicity. In addition, immunization with PSs does not induce high affinity antibody production and no memory *B"**-*cells"** are generated. Coupling PSs to carrier proteins has been reported to induce *B"**-*cell"** maturation and to install a *B"**-*cell"** memory. As an alternative carrier protein, the *outer"** *membrane"** *protein"** *A"** (*OmpA"**) derived from *Klebsiella"** *pneumoniae"** has been coupled to various PSs. We evaluated the immunogenicity of two PS conjugates, using PS derived from S. pneumoniae types 14 and 19. In this report, we show that anti-PS IgG responses are generated after the conjugation of PSs to P40. In addition, the humoral response generated is able to protect mice from a bacterial challenge. Our results indicate that P40 could be included in the development of new PS conjugate vaccines.

4/3,AB/3 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

15622143 PASCAL No.: 02-0326401
Targeting of nasal mucosa-associated *antigen"**-presenting *cells"** in vivo with an *outer"** *membrane"** *protein"** *A"** derived from

*Klebsiella"** *pneumoniae"**
GOETSCH Liliane; GONZALEZ Alexandra; PLOTNICKY-GILQUIN Helene; HAEUW Jean Francois; AUBRY Jean Pierre; BECK Alain; BONNEFOY Jean Yves; CORVAIA Nathalie
Centre d'Immunologie Pierre Fabre, 74164 Saint-Julien en Genevois, France
Journal: Infection and immunity, 2001, 69 (10) 6434-6444
Language: English
Administration of vaccines by the nasal route has recently proven to be one of the most efficient ways for inducing both mucosal and systemic antibody responses in experimental animals. Our results demonstrate that P40, a well-defined *outer"** *membrane"** *protein"** *A"** from *Klebsiella"** *pneumoniae"** , is indeed a carrier molecule suitable for nasal immunization. Using fragments from the respiratory syncytial virus subgroup A (RSV-A) G protein as antigen models, it has been shown that P40 is able to induce both systemic and mucosal immunity when fused or coupled to a protein or a peptide and administered intranasally (i.n.) to naive or *K"**. *pneumoniae"** -primed mice. Confocal analyses of nasal mucosa-associated lymphoid tissue after i.n. instillation of P40 showed that this molecule is able to cross the nasal epithelium and target CD11c-positive cells likely to be murine *dendritic"** cells or macrophages. More importantly, this targeting of *antigen"**-presenting *cells"** following i.n. immunization with a subunit of the RSV-A molecule in the absence of any mucosal adjuvant results in both upper and lower respiratory tract protection against RSV-A infection.

4/3,AB/4 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

14323680 PASCAL No.: 99-0531767
Carrier properties of a protein derived from *outer"** *membrane"** *protein"** *A"** of *Klebsiella"** *pneumoniae"**
RAULY I; GOETSCH L; HAEUW J F; TARDIEUX C; BAUSSANT T; BONNEFOY J Y; CORVAIA N
Centre d'Immunologie Pierre Fabre, Saint Julien en Genevois, France
Journal: Infection and immunity, 1999, 67 (11) 5547-5551
Language: English
We have recently cloned a new protein, recombinant P40 (rP40). When tested in vivo after conjugation to a *B"**-*cell"** epitope, rP40 induces an important antibody response without the need for adjuvant. To characterize its potency, this carrier protein was coupled to a peptide derived from respiratory syncytial virus attachment G protein (G1'). After immunization of mice with the rP40-G1' conjugate, strong antipeptide antibodies were detected, whereas peptide alone was not immunogenic. To emphasize the carrier properties of rP40, a polysaccharide derived from Haemophilus influenzae type b (Hib) was coupled to it. Immunoglobulin G responses against the Hib polysaccharide were observed after coupling to rP40. Interestingly, an antipeptide antibody response was observed despite preexisting anti-rP40 antibodies generated by preimmunization with rP40. In addition, rP40 compares well with the reference carrier protein, tetanus toxoid (TT), since antibody responses of equal intensity were observed when a peptide or a polysaccharide was coupled to TT and rP40. Moreover, rP40 had advantages compared to TT; e.g., it induced a mixed Th1/Th2 response, whereas TT induced only a Th2 profile. Together, the results indicate that rP40 is a novel carrier protein with potential for use as an alternative

carrier for human vaccination.

4/3,AB/5 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

12551396 PASCAL No.: 96-0231729
P40, la proteine majeure de la membrane externe de *Klebsiella"** *Pneumoniae"** I-145: clonage, expression de la proteine recombinante et localisation des domaines responsables de l'activite adjuvante
(P40, the major outer membrane protein of *Klebsiella"** *Pneumoniae"** I-145: clonge, expression of the recombinante protein and localisation of the parts involve in the adjuvant activity)
MERLE-POITTE MERLE Christine; AILHAUD G, dir
Universite de Nice, Nice, Francee
Univ.: Universite de Nice. Nice. FRA Degree: Th. doct.
1995-11; 1995 132 p.
Language: French Summary Language: French; English
L'utilisation de molecules peu immunogeniques, peptides ou oligosaccharides, dans l'elaboration de nouveaux vaccins, necessite une association a une proteine porteuse et a un adjuvant pour obtenir une reponse immunologique. P40, l'*OmpA"** de Kelbsiella pneumoniae I-145 presente des proprietes de porteur/adjuvant, demontrees a l'aide de conjugues realises avec differents antigenes: peptides et oligosaccharides. Afin d'utiliser P40 dans la preparation de vaccins, nous avons recherche les sequences impliquees dans l'activite adjuvante de la proteine. Le gene de P40, de 1008 paires de bases, a ete clone et sequence. La proteine recombinante a ete exprimee dans E. coli sous la forme des produits de fusion BBP40 et BBP40G2 triangle C. Ces proteines presentent des proprietes immunologiques analogues a celles de la proteine d'extraction. Pour localiser les sequences responsables du pouvoir adjuvant de P40, trois fragments (1-179, 108-179, 118-179) ont ete clones et exprimes sous la forme BB triangle P40G2 triangle C. Les etudes menees avec ces proteines de fusion ont montre que la partie membranaire rendait compte a elle seule du pouvoir adjuvant de P40. L'antigenicite de la proteine reside au niveau du domaine periplasmique et de la premiere moitie du domaine membranaire. Comme le ciblage de l'antigene sur les cellules presentatrices d'antigene est une facon de potentialiser une reponse immunitaire, nous avons etudie l'interaction de P40 avec une lignee de *monocytes"**-macrophages. L'etude a ete realisee par immunomarquage puis analyse par cytofluorimetrie. P40 interagit directement avec la cellule en se fixant a sa surface. La fixation est rapide. Elle est demontree sur les macrophages, les splenocytes et les cellules de myelome. L'interaction de P40 avec les *monocytes"** -macrophages se fait par une structure exprimee a la surface des cellules et qui reste a definir. L'identification et l'utilisation des sequences de P40 responsables des proprietes adjuvante et porteuse devraient

4/3,AB/6 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

11318574 PASCAL No.: 94-0139571
The 39-kilodalton outer membrane protein of Proteus mirabilis is an

*OmpA"** protein and mitogen for murine *B"** *lymphocytes"**
KORN A; KROLL H P; BERGER H P; KAHLER A; HESSLER R; BRAUBURGER J; MUELLER K P; NIXDORFF K
Univ. Darmstadt, dep. microbiology, 64287 Darmstadt, Federal Republic of Germany
Journal: Infection and immunity, 1993, 61 (11) 4915-4918
Language: English
Partial amino acid sequence analysis of a major outer membrane protein of Proteus mirabilis (39-kDa protein) indicates that it is an *OmpA"** protein. The mitogenic activities of the 39-kDa protein for murine lymphocytes were also investigated with T lymphocytes isolated by passing spleen cells over columns of nylon wool fiber and *B"** *lymphocytes"** obtained by treating spleen cells with monoclonal antibodies to Thy1 plus complement. The 39-kDa protein showed little activity in stimulating T cells to proliferate but was strongly mitogenic for *B"** *cells"**

4/3,AB/7 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

16175810 Document Delivery Available: 000182847700005 References: 33
TITLE: *Outer"** *membrane"** *protein"** *A"** (*OmpA"**) activates human epidermal Langerhans cells
AUTHOR(S): Godefroy S; Corvaia N; Schmitt D; Aubry JP; Bonnefoy JY; Jeannin P; Staquet MJ (REPRINT)
AUTHOR(S) E-MAIL: u346@lyon.inserm.fr
CORPORATE SOURCE: Hop Edouard Herriot, U346, /F-69437 Lyon//France/ (REPRINT); Hop Edouard Herriot, U346, /F-69437 Lyon//France/; Ctr Immunol Pierre Fabre, /St Julien En Genevois//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: EUROPEAN JOURNAL OF CELL BIOLOGY, 2003, V82, N4 (APR), P 193-200
GENUINE ARTICLE#: 678CP
PUBLISHER: URBAN & FISCHER VERLAG, BRANCH OFFICE JENA, P O BOX 100537, D-07705 JENA, GERMANY
ISSN: 0171-9335
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Outer membrane protein (*Omp"**)*A"** is highly represented and conserved in the *Enterobacteriaceae"** family. Using a recombinant *OmpA"** from *Klebsiella"** *pneumoniae"** (*kpOmpA"**), we have analysed the interaction between this bacterial cell wall protein and human Langerhans cells (LC), the *antigen"**-presenting *cells"** of the epidermis and mucosa. We showed that biotinylated *kpOmpA"** binds to human LC freshly isolated from epidermis. *kpOmpA"** up-regulated MHC class 11, CD86 and CCR7 expression, enhanced migration in response to macrophage inflammatory protein-3beta (MIP-3beta) through a reconstituted basement membrane mimicking the prerequisite passage through the dermal-epidermal basement membrane on the way to lymph nodes. The allostimulatory function of *kpOmpA"**-treated LC was more potent than that of untreated cells. Even though the proportion of LC which binds *kpOmpA"** was shown to vary between individuals, our data indicate that *kpOmpA"** binds to and activates LC, and suggest that recognition of *OmpA"** by LC may be an initiating event in the antibacterial host response.

4/3,AB/8 (Item 2 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

15618239 Document Delivery Available: 000180988100006 References: 31
TITLE: *Outer"** *membrane"** *protein"** *A"** renders *dendritic"** cells and macrophages responsive to CCL21 and triggers *dendritic"** cell migration to secondary lymphoid organs
AUTHOR(S): Jeannin P (REPRINT); Magistrelli G; Herbault N; Goetsch L; Godefroy S; Charbonnier P; Gonzalez A; Delneste Y
AUTHOR(S) E-MAIL: pascale.jeannin@pierre-fabre.com
CORPORATE SOURCE: Ctr Immunol Pierre Fabre, 5 Ave Napoleon III/F-74160 St Julien en Genevois//France/ (REPRINT); Ctr Immunol Pierre Fabre, /F-74160 St Julien en Genevois//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: EUROPEAN JOURNAL OF IMMUNOLOGY, 2003, V33, N2 (FEB), P326-333
GENUINE ARTICLE#: 645PT
PUBLISHER: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY
ISSN: 0014-2980
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: *Outer"** *membrane"** *protein"** *A"** (*OmpA"**) is a class of bacterial cell wall protein that is immunogenic without adjuvant. As specific immune responses are initiated in the lymph nodes (LN), we analyzed the effect of the *OmpA"** from *Klebsiella"** *pneumoniae"** (*KpOmpA"**) on chemokine/ chemokine receptor expression by APC and on cell migration to the LN. Upon contact with *KpOmpA"**, human immature DC and macrophages acquire CCR7 expression and responsiveness to CCL21. In parallel, CCR1 and CCR5 expression is down-regulated and CXCL8, CCL2, CCL3 and CCL5 production is up-regulated. Mice injected subcutaneously with *KpOmpA"** present a transient inflammatory reaction at the site of injection accompanied by an enlargement of the draining LN with a higher proportion of DC and macrophages. Lastly, when exposed to *KpOmpA"** prior injection, DC but not macrophages migrate to the draining LN. In conclusion, *KpOmpA"** confers a migratory phenotype to DC and triggers their migration to the regional LN. This property contributes to explain how innate cells initiate adaptive immune response upon recognition of conserved bacterial components and also why *OMPA"** is immunogenic in the absence of adjuvant.

4/3,AB/9 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13426049 References: 12
TITLE: Stability and CTL-activity of P40/ELA melanoma vaccine candidate
AUTHOR(S): Beck A (REPRINT); Goetsch L; Champion T; Bussat MC; Aubry JP; Klinguer-Hamour C; Haeuw JF; Bonnefoy JY; Corvaia N
AUTHOR(S) E-MAIL: alain.beck@pierre-fabre.com
CORPORATE SOURCE: BioMerieux Pierre Fabre, Dept Physicochem, 5 Ave Napoleon 3,BP 497/F-74164 St Julien En Genevois//France/ (REPRINT); BioMerieux Pierre Fabre, Dept Physicochem, /F-74164 St Julien En Genevois//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: BIOLOGICALS, 2001, V29, N3-4 (SEP-DEC), P293-298
GENUINE ARTICLE#: 512ZA
PUBLISHER: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND
ISSN: 1045-1056

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The decapeptide ELA (ELAGIGILTV), a Melan-A/MART-1 antigen immunodominant peptide analogue, is an interesting melanoma vaccine candidate alone or in combination with other tumour antigens. P40, the recombinant *outer"** *membrane"** *protein"** *A"** of *Klebsiella"** *pneumoniae"** (*kpOmpA"**), was recently shown to target *dendritic"** cells and to induce peptide-specific CTLs. Here we investigated the adjuvant role of P40 mixed or chemically conjugated to ELA. This compound is an N-terminal glutamic acid-containing peptide. However, it has been reported that the amino group and the gamma-carboxylic group of glutamic acids easily condense to form pyroglutamic derivatives. Usually, to overcome this stability problem, peptides of pharmaceutical interest were developed with a pyroglutamic acid instead of N-terminal glutamic acid, without loss of pharmacological properties. Unfortunately, the pyroglutamic acid derivative (PyrELA) as well as the N-terminal acetyl capped derivative (AcELA) failed to elicit CTL activity when mixed with P40 adjuvant protein. Despite the apparent minor modifications introduced by PyrELA and AcELA, these two derivatives have probably lower affinity than ELA for the class I Major Histocompatibility Complex. Furthermore, this stability problem is worse in the case of clinical grade ELA, produced as an acetate salt, like most of the pharmaceutical grade peptides. We report here that the hydrochloride shows a higher stability than the acetate and may be suitable for use in man. (C) 2001 The International Association for Biologicals.

4/3,AB/10 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12237080 References: 53
TITLE: *OmpA"** targets *dendritic"** cells, induces their maturation and delivers antigen into the MHC class I presentation pathway
AUTHOR(S): Jeannin P (REPRINT); Renno T; Goetsch L; Miconnet I; Aubry JP; Delneste Y; Herbault N; Baussant T; Magistrelli G; Soulas C; Romero P; Cerottini JC; Bonnefoy JY
AUTHOR(S) E-MAIL: pascale.jeannin@pierre-fabre.com
CORPORATE SOURCE: Ctr Immunol Pierre Fabre, 5 Ave Napoleon III/F-74164 St Julien en Genevois//France/ (REPRINT); Ctr Immunol Pierre Fabre, /F-74164 St Julien en Genevois//France/; Univ Lausanne, Ludwig Inst Canc Res, /CH-1406 Epalinges//Switzerland/
PUBLICATION TYPE: JOURNAL
PUBLICATION: NATURE IMMUNOLOGY, 2000, V1, N6 (DEC), P502-509
GENUINE ARTICLE#: 380VR
PUBLISHER: NATURE AMERICA INC, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707 USA
ISSN: 1529-2908
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We analyzed the interaction between a bacterial cell wall protein and *dendritic"** cells (DCs), *Outer"** *membrane"** *protein"** *A"** from *Klebsiella"** *pneumoniae"** (*kpOmpA"**) specifically bound to professional *antigen"** presenting *cells"** and was endocytosed by immature DCs via a receptor-dependent mechanism. *kpOmpA"** signaled through Toll like receptor 2, induced DCs to produce interleukin 12 and induced maturation of DCs,Whole antigen that was coupled to *kpOmpA"** and injected into mice was taken up by DCs and delivered to the conventional cytosolic MHC class I presentation pathway. *kpOmpA"** also primed

antigen-specific CD8(+) CTLs in the absence of CD4(+) T cell help or adjuvant and elicited therapeutic immunity to antigen-expressing tumors. Thus, *OmpA"** belongs to a class of proteins that are able to elicit CTL responses to exogenous antigen.

4/3,AB/11 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01438197
CD2000 and CD2001 molecules and uses thereof
CD2000 und CD2001 Molekule und deren Verwendungen
Molecules CD2000 et CD2001 et utilisations de celles-ci
PATENT ASSIGNEE:
Millennium Pharmaceuticals, Inc., (2190396), 75 Sidney Street, Cambridge, Massachusetts 02139, (US), (Applicant designated States: all)
INVENTOR:
Fraser, Christopher C., 53 Grassland Street, Lexington, MA 02421, (US)
LEGAL REPRESENTATIVE:
Jump, Timothy John Simon et al (55592), Venner Shipley & Co. 20 Little Britain, London EC1A 7DH, (GB)
PATENT (CC, No, Kind, Date): EP 1223218 A1 020717 (Basic)
APPLICATION (CC, No, Date): EP 2001309339 011102;
PRIORITY (CC, No, Date): US 706167 001103
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/12; C07K-014/705; C12N-005/00; C12N-015/62; G01N-033/50; G01N-033/53; C12Q-001/68; A61K-039/395
ABSTRACT EP 1223218 A1
The invention provides isolated nucleic acid molecules, designated CD2000, which encode polypeptide molecules containing Ig and Ig-like domains and SLAM associated protein (SAP) motifs. The invention also provides isolated nucleic acid molecules, designated CD2001, which encode polypeptide molecules containing an Ig and Ig-like domains. The invention also provides antisense nucleic acid molecules, expression vectors containing the nucleic acid molecules of the invention, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a nucleic acid molecule of the invention has been introduced or disrupted. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides and antibodies. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.
ABSTRACT WORD COUNT: 117

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200229	1252
SPEC A	(English)	200229	56836
Total word count - document A			58088
Total word count - document B			0
Total word count - documents A + B			58088

4/3,AB/12 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01169143
USE OF AN *ENTEROBACTERIUM"** PROTEIN *OmpA"** FOR SPECIFIC TARGETING TOWARDS *ANTIGEN"**-PRESENTING *CELLS"**
VERWENDUNG VON *OmpA"** ENTEROBAKTERPROTEINEN FUR SPECIFISCHE ZIELRICHTUNG NACH ANTIGEN PRASENTIRENDEN ZELLEN
UTILISATION D'UNE PROTEINE *OmpA"** D'*ENTEROBACTERIE"**, POUR LE CIBLAGE SPECIFIQUE VERS LES CELLULES PRESENTATRICES D'ANTIGENES
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)
INVENTOR:
BONNEFOY, Jean-Yves, Les Noyers, F-74350 Le Sappey, (FR)
LECOANET, Sybille, 41, A1 Residence du Golf, CH-1196 Gland, (CH)
AUBRY, Jean-Pierre, 60, chemin des Crets des Crets, F-74350 Cuvat, (FR)
JEANNIN, Pascale, 135, chemin de Revule, F-01220 Divonne-les-Bains, (FR)
BAUSSANT, Thierry, 4 rue Alphonse Baudin, F-01200 Bellegarde, (FR)
LEGAL REPRESENTATIVE:
Ahner, Francis et al (13603), Cabinet Regimbeau, 20, rue de Chazelles, 75847 Paris Cedex 17, (FR)
PATENT (CC, No, Kind, Date): EP 1124577 A1 010822 (Basic)
WO 200027432 000518
APPLICATION (CC, No, Date): EP 99971719 991108; WO 99FR2734 991108
PRIORITY (CC, No, Date): FR 9814007 981106
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/39; A61P-031/00; A61P-035/00; A61P-037/00
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): French; French; French

4/3,AB/13 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01042334
Method to determine biomolecular interaction
Verfahren zum Biomolekularinteraktionsnachweis
Methode pour determiner d'action reciproque biomoleculaire
PATENT ASSIGNEE:
von Gabain, Alexander, (2426210), Hockegasse 77, 1180 Wien, (AT), (Proprietor designated states: all)
Hirsh, Aaron, (2426220), 1003 Rosehill Drive, Boulder, CO 80302, (US), (Proprietor designated states: all)
INVENTOR:
von Gabain, Alexander, Hockegasse 77, 1180 Wien, (AT)
Hirsh, Aaron, 1003 Rosehill Drive, Boulder, CO 80302, (US)
LEGAL REPRESENTATIVE:
Alge, Daniel, Mag. Dr. rer.nat. et al (79841), Patentanwalte Sonn, Pawloy, Weinzinger & Kohler-Pavlik Riemergasse 14, 1010 Wien, (AT)
PATENT (CC, No, Kind, Date): EP 922957 A1 990616 (Basic)
EP 922957 B1 000329
APPLICATION (CC, No, Date): EP 97121451 971205;
PRIORITY (CC, No, Date): EP 97121451 971205
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; IT; LI; NL; SE

EXTENDED DESIGNATED STATES: SI
INTERNATIONAL PATENT CLASS: G01N-033/48; G01N-033/50; G01N-033/569; G01N-033/68

ABSTRACT EP 922957 A1
This invention is a method for determining the interaction of a target compound with a (poly)peptide of interest (which is selected from proteins, glycoproteins, or proteoglycans or sections thereof) exhibiting specific, prescribed properties. The interaction is characterized by at least one of the interactants being unknown. In general, only one of the interactants is unknown.

When the unknown interactant is the (poly)peptide of interest, the method is based on three components: (1) a population of prokaryotic or eukaryotic cells displaying on their surface a combinatorial library in one protein, glycoprotein, or proteoglycan; (2) a target compound; and (3) a toxic agent. Interaction among the three components "imprints" the combinatorially varied polypeptide: that is, the interaction selects for those cells in which the combinatorially varied polypeptide interacts with the target compound in a prescribed manner.
ABSTRACT WORD COUNT: 136
NOTE:
Figure number on first page: 7

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200013	878
CLAIMS B	(German)	200013	875
CLAIMS B	(French)	200013	960
SPEC B	(English)	200013	33079
Total word count - document A			0
Total word count - document B			35792
Total word count - documents A + B			35792

4/3,AB/14 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00803306
EXPRESSION OF PROTEINS ON BACTERIAL SURFACE
EXPRESSION VON PROTEINEN AUF DER OBERFLACHE VON BAKTERIEN
EXPRESSION DE PROTEINES SUR LA SURFACE DE BACTERIES
PATENT ASSIGNEE:
GEORGIOU, George, (1657030), 11501 Juniper Ridge Drive, Austin, TX 78759, (US), (Proprietor designated states: all)
INVENTOR:
GEORGIOU, George, 11501 Juniper Ridge Drive, Austin, TX 78759, (US)
FRANCISCO, Joseph, A., 9901 Chukar Circle, Austin, TX 78758, (US)
EARHART, Charles, F., 2702 Mt. Laurel Drive, Austin, TX 78703, (US)
LEGAL REPRESENTATIVE:
Dost, Wolfgang, Dr.rer.nat., Dipl.-Chem. et al (3042), Patent- und Rechtsanwalte Bardehle . Pagenberg . Dost . Altenburg . Geissler . Isenbruck Postfach 86 06 20, 81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 746621 A1 961211 (Basic)
EP 746621 B1 020327
WO 9310214 930527

APPLICATION (CC, No, Date): EP 93909521 921110; WO 92US9756 921110
PRIORITY (CC, No, Date): US 794731 911115
DESIGNATED STATES: BE; CH; DE; FR; GB; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/62; C12N-015/70; C12N-015/74; C12N-001/21; A61K-039/00; C07K-001/00; C12N-011/16; C07K-014/00; C12R-1:19; C12R-1:01
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200213	795
CLAIMS B	(German)	200213	787
CLAIMS B	(French)	200213	946
SPEC B	(English)	200213	10544
Total word count - document A			0
Total word count - document B			13072
Total word count - documents A + B			13072

4/3,AB/15 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00712934
Antibodies to mammalian interleukin-4 and peptides useful as antigens in their production
Antikorper gegen Saugetier-Interleukin-4 und Peptide verwendbar als Antigenen fur deren Herstellung
Anticorps contre l'interleukine-4 de mammiferes et peptides utiles comme antigenes pour leur preparation
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (Proprietor designated states: all)
INVENTOR:
Lee, Frank, 212 Rinconada Avenue, Palo Alto, California 94301, (US)
Yokota, Takashi, 890 Colorado Avenue, Palo Alto, California 94303, (US)
Arai, Ken-ichi, 648 Georgia Avenue, Palo Alto, California 94306, (US)
Mosmann, Timothy, 69 Lloyden Drive, Atherton, California 94025, (US)
Rennick, Donna, 601 Almond Avenue, Los Altos, California 94022, (US)
Smith, Craig, 350 Franklin Street, Mountain View, California 94041, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 675136 A2 951004 (Basic)
EP 675136 A3 960313
EP 675136 B1 010117
APPLICATION (CC, No, Date): EP 95108150 861119;
PRIORITY (CC, No, Date): US 799668 851119; US 799669 851119; US 843958 860325; US 881553 860703; US 908215 860917
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 249613 (EP 86907184)
INTERNATIONAL PATENT CLASS: C07K-016/24; C07K-014/54; A61K-039/395; G01N-033/68

ABSTRACT EP 675136 A2
Antibodies to mammalian Interleukin-4 and muteins are provided,

especially to native human IL-4s, as well as peptides useful as antigens in their production. Nucleic acids are disclosed which are capable of coding for the mammalian IL-4s and their muteins.
ABSTRACT WORD COUNT: 50
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200103	1231
CLAIMS B	(German)	200103	1240
CLAIMS B	(French)	200103	1313
SPEC B	(English)	200103	26698
Total word count - document A			0
Total word count - document B			30482
Total word count - documents A + B			30482

4/3,AB/16 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00648931
ANTHRAX TOXIN FUSION PROTEINS AND USES THEREOF
ANTHRAX-TOXIN-FUSIONSPROTEINE UND DEREN VERWENDUNGEN
PROTEINES DE FUSION DE LA TOXINE DU BACILLE DU CHARBON ET LEURS UTILISATIONS
PATENT ASSIGNEE:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by the SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, (304190), National Institute of Health, Office of Technology Transfer, Westwood Building, Box OTT, Bethesda, MD 20892-9902, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
LEPPLA, Stephen H., 5612 Alta Vista Road, Bethesda, MD 20817, (US)
KLIMPEL, Kurt, 23816 Woodfield Road, Gaithersburg, MD 20882, (US)
ARORA, Naveen, G 110 Ashok Vihar, Phase I, Delhi 110052, (IN)
SINGH, Yogendra, SCIR Center for Biochemicals, University of Delhi, Mall Road, Delhi 110007, (IN)
LEGAL REPRESENTATIVE:
Thomson, Paul Anthony et al (36701), Potts, Kerr & Co. 15, Hamilton Square, Birkenhead Merseyside L41 6BR, (GB)
PATENT (CC, No, Kind, Date): EP 684997 A1 951206 (Basic)
EP 684997 B1 980819
WO 9418332 940818
APPLICATION (CC, No, Date): EP 94911385 940214; WO 94US1624 940214
PRIORITY (CC, No, Date): US 21601 930212; US 82849 930625
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/62; C12N-015/85; C12N-015/32; C07K-014/00; A61K-039/02; A61K-038/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9834	168

CLAIMS B	(German)	9834	134
CLAIMS B	(French)	9834	198
SPEC B	(English)	9834	21580
Total word count - document A			0
Total word count - document B			22080
Total word count - documents A + B			22080

4/3,AB/17 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00628750
METHODS AND COMPOSITIONS RELATING TO USEFUL ANTIGENS OF MORAXELLA CATARRHALIS
VERFAHREN UND ZUSAMMENSETZUNGEN IM HINBLICK AUF NUTZLICHE MORAXELLA CATARRHALIS ANTIGENE
PROCEDES ET COMPOSITIONS RELATIFS A DES ANTIGENES UTILES DE MORAXELLA CATARRHALIS
PATENT ASSIGNEE:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM, (266340), 201 West 7th Street, Austin, Texas 78701, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;SE)
INVENTOR:
HANSEN, Eric, J., 2404 Chamberlain, Plano, TX 75023, (US)
HELMINEN, Merja, 6031 Pineland 1116, Dallas, TX 75231, (US)
MACIVER, Isobel, 6721 Larmanda, Suite 254, Dallas, TX 75231, (US)
LEGAL REPRESENTATIVE:
Dost, Wolfgang, Dr.rer.nat., Dipl.-Chem. et al (3049), Patent- und Rechtsanwalte Bardehle . Pagenberg . Dost . Altenburg . Frohwitter . Geissler & Partner Galileiplatz 1, 81679 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 612250 A1 940831 (Basic)
EP 612250 B1 960724
WO 9303761 930304
APPLICATION (CC, No, Date): EP 92918273 920814; WO 92US6869 920814
PRIORITY (CC, No, Date): US 745591 910815
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; C12N-015/31; C12P-021/08; C07K-002/00; G01N-033/569; G01N-033/577; A61K-038/00; A61K-039/395;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	925
CLAIMS B	(German)	EPAB96	904
CLAIMS B	(French)	EPAB96	1017
SPEC B	(English)	EPAB96	13921
Total word count - document A			0
Total word count - document B			16767
Total word count - documents A + B			16767

4/3,AB/18 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00584422
USE OF INTERLEUKIN-10 ANALOGS OR ANTAGONISTS TO TREAT ENDOTOXIN- OR SUPERANTIGEN INDUCED TOXICITY
VERWENDUNG VON INTERLEUKIN-10 ANALOGEN ODER ANTAGONISTEN ZUR BEHANDLUNG VON ENDOTOXIN- ODER SUPERANTIGEN INDUZIERTER TOXIZITAT
UTILISATION D'ANALOGUES OU D'ANTAGONISTES DE L'INTERLEUKINE-10 POUR TRAITER LA TOXICITE INDUITE PAR L'ENDOTOXINE OU UN SUPERANTIGENE
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (Proprietor designated states: all)
INVENTOR:
DE WAAL MALEFYT, Rene, 1921 California Street, 12, Mountain View, CA 94040, (US)
HOWARD, Maureen, 12700 Viscaino Drive, Los Altos Hills, CA 94022, (US)
HSU, Di-Hwei, 350 Curtner Avenue, Palo Alto, CA 94306, (US)
ISHIDA, Hiroshi, 1-6-9, Sekido B-201, Wakayama City Wakayama 641, (JP)
O'GARRA, Anne, 1094 Tanland Drive, 106, Palo Alto, CA 94303, (US)
SPITS, Hergen, 3271 Murray Way, Palo Alto, CA 94303, (US)
ZLOTNIK, Albert, 507 Alger Drive, Palo Alto, CA 94306, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 600970 A1 940615 (Basic)
EP 600970 B1 991208
WO 9302693 930218
APPLICATION (CC, No, Date): EP 92917650 920806; WO 92US6378 920806
PRIORITY (CC, No, Date): US 742129 910806
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/00; A61K-039/395
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9949	429
CLAIMS B	(German)	9949	420
CLAIMS B	(French)	9949	477
SPEC B	(English)	9949	32967
Total word count - document A			0
Total word count - document B			34293
Total word count - documents A + B			34293

4/3,AB/19 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00556890
USE OF INTERLEUKIN-10 IN ADOPTIVE IMMUNOTHERAPY OF CANCER.
VERWENDUNG VON INTERLEUKIN-10 IN DER ADOPTIVE IMMUNOTHERAPIE VON KREBS.
EMPLOI DE L'INTERLEUKINE-10 DANS L'IMMUNOTHERAPIE ADOPTIVE DU CANCER.
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
HSU, Di-Hwei, 1815 Latham Street 15, Mountain View, CA 94041, (US)

MOORE, Kevin, W., 4144 Park Boulevard, Palo Alto, CA 94306, (US)
SPITS, Hergen, General Snijdersplantsoenzg, Badhoevedorp 1171 HN, (NL)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 567586 A1 931103 (Basic)
EP 567586 B1 950712
WO 9212726 920806
APPLICATION (CC, No, Date): EP 92905179 920115; WO 92US67 920115
PRIORITY (CC, No, Date): US 641342 910116
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-038/20; C12N-005/08; C12N-015/24
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	278
CLAIMS B	(German)	EPAB95	269
CLAIMS B	(French)	EPAB95	328
SPEC B	(English)	EPAB95	7621
Total word count - document A			0
Total word count - document B			8496
Total word count - documents A + B			8496

4/3,AB/20 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00556664
TREATMENT OF NEOPLASTIC DISEASE WITH INTERLEUKIN-10.
BEHANDLUNG VON NEOPLASTISCHEN KRANKENHEITEN MIT INTERLEUKIN-10.
TRAITEMENT DE MALADIE NEOPLASTIQUE A L'INTERLEUKINE 10.
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
INVENTOR:
VIEIRA, Paulo, J., M., 178 Centre Street, 18, Mountain View, CA 94041, (US)
MOORE, Kevin, W., 4144 Park Boulevard, Palo Alto, CA 94306, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 567576 A1 931103 (Basic)
WO 9212725 920806
APPLICATION (CC, No, Date): EP 92904687 920115; WO 92US66 920115
PRIORITY (CC, No, Date): US 641347 910116
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: A61K-038/20
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count

CLAIMS B	(English)	EPBBF2	102
CLAIMS B	(German)	EPBBF2	74
CLAIMS B	(French)	EPBBF2	77
SPEC B	(English)	EPBBF2	8524
Total word count - document A			0
Total word count - document B			8777
Total word count - documents A + B			8777

4/3,AB/21 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00536086
Use of interleukin-10 in adoptive immunotherapy of cancer.
Verwendung von Interleukin-10 in der adaptiven Immunotherapie von Krebs.
Utilisation de l'interleukine-10 dans l'immunotherapie adoptive du cancer.
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: PT)
INVENTOR:
Hsu, Di-Hwei, 1815 Latham Street No.15, Mountain View, California 94041, (US)
Moore, Kevin W., 4144 Park Boulevard, Palo Alto, California 94306, (US)
Spits, Hergen, 3271 Murray Way, Palo Alto, California 94303, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 495639 A1 920722 (Basic)
APPLICATION (CC, No, Date): EP 92300331 920115;
PRIORITY (CC, No, Date): US 641342 910116
DESIGNATED STATES: PT
INTERNATIONAL PATENT CLASS: A61K-037/02; C12N-005/08; C12N-015/24
ABSTRACT EP 495639 A1
A method is provided for using interleukin-10 in adoptive immunotherapy of cancer. A population of tumor-infiltrating lymphocytes (TILs) are expanded in culture in the presence of interleukin-2 (IL-2) and interleukin-10 (IL-10). After administration of the TILs to a patient, effective amounts of both IL-2 and IL-10 are administered to enhance the tumor-cell cytoxicity of the TILs and to reduce side-effects caused by IL-2-induced cytokine production in the TILs and other cells of the patient.
ABSTRACT WORD COUNT: 76

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	351
SPEC A	(English)	EPABF1	7624
Total word count - document A			7975
Total word count - document B			0
Total word count - documents A + B			7975

4/3,AB/22 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00450224
CYTOKINE SYNTHESIS INHIBITORY FACTOR AND METHODS OF USING SAME
CYTOKINSYNTHESEHEMMENDER FAKTOR (CSIF) UND VERFAHREN ZUR ANWENDUNG
FACTEUR INHIBITEUR DE LA SYNTHESE DE CYTOKINES AINSI QUE SES PROCEDES D'UTILISATION
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
MOSMANN, Timothy, R. 26 Wedgewood Crescent, Box 63, Site 2, R.R. 5, Edmonton, Alberta T5P 4B7, (CA)
MOORE, Kevin, W., 4144 Park Boulevard, Palo Alto, CA 94306, (US)
BOND, Martha, W., 4229 McKellar Lane, Palo Alto, CA 94036, (US)
VIEIRA, Paulo, J., M., 178 Centre Street, 18, Mountain View, CA 94041, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 567450 A1 931103 (Basic)
EP 567450 B1 990602
WO 9100349 910110
APPLICATION (CC, No, Date): EP 90911213 900628; WO 90US3554 900628
PRIORITY (CC, No, Date): US 372667 890628; US 453951 891220
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/24; C12N-015/70; C12N-015/85; C07K-014/00; C12P-021/08;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9922	695
CLAIMS B	(German)	9922	669
CLAIMS B	(French)	9922	765
SPEC B	(English)	9922	12153
Total word count - document A			0
Total word count - document B			14282
Total word count - documents A + B			14282

4/3,AB/23 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00431158
Cytokine synthesis inhibitory factor, antagonists thereof, and methods of using same.
Cytokinsynthesehemmender Faktor-(CSIF), Antagonisten dafur und Verfahren zur Anwendung.
Facteur inhibant la synthese de cytokine (CSIF), antagonistes et utilisations.
PATENT ASSIGNEE:
SCHERING CORPORATION, (240551), 2000 Galloping Hill Road, Kenilworth New Jersey 07033, (US), (applicant designated states: GR)
INVENTOR:
Mosmann, Timothy R., 26 Wedgewood Crescent, Box 63, Site 2, R.R 5, Edmonton, Alberta T5P 4B7, (CA)

Moore, Kevin W., 4144 Park Boulevard, Palo Alto, California 94306, (US)
Bond, Martha W., 4229 McKellar Lane, Palo Alto, California 94306, (US)
Vieira, Paulo J.M., 178 Centre Street, 18, Mountain View, California 94041, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 405980 A1 910102 (Basic)
APPLICATION (CC, No, Date): EP 90307091 900628;
PRIORITY (CC, No, Date): US 372667 890628; US 453951 891220
DESIGNATED STATES: GR
INTERNATIONAL PATENT CLASS: C12N-015/24; C07K-013/00; C12N-015/70; C12N-015/85; C12P-021/08;

ABSTRACT EP 405980 A1
Mammalian genes and proteins, designated cytokine synthesis inhibitory factors (CSIFs), are provided which are capable of inhibiting the synthesis of cytokines associated with delayed type hypersensitivity responses, and which, together with antagonists, are useful in treating diseases associated with cytokine imbalances, such as leishmaniasis and other parasitic infections, and certain immune disorders including MHC associated autoimmune diseases caused by excessive production of interferon-(gamma).
ABSTRACT WORD COUNT: 67

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	974
SPEC A	(English)	EPABF1	12428
Total word count - document A			13402
Total word count - document B			0
Total word count - documents A + B			13402

4/3,AB/24 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00319308
Human Fc-gamma receptor.
Menschlicher Fc-gamma-Rezeptor.
Recepteur Fc-gamma humain.
PATENT ASSIGNEE:
Schering Biotech Corporation, (636051), 901 California Avenue, Palo Alto California 94304-1104, (US), (applicant designated states: ES;GR)
INVENTOR:
Moore, Kevin W., 4144 Park Blvd., Palo Alto California 94306, (US)
Peltz, Gary A., 1145 Divisadero Street Apt. No. 3, San Francisco California 94115, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 319307 A2 890607 (Basic)
EP 319307 A3 890830
APPLICATION (CC, No, Date): EP 88311408 881201;
PRIORITY (CC, No, Date): US 129002 871204
DESIGNATED STATES: ES; GR

INTERNATIONAL PATENT CLASS: C12N-015/00; A61K-037/02; G01N-033/566;
ABSTRACT EP 319307 A2

A cDNA clone is provided which encodes a human receptor for the Fc portion of immunoglobulin G. Soluble forms of the receptor may be useful in treating disorders associated with excessive immunoglobulin G production. Cells expressing membrane-bound forms of the receptor are useful in assays for immune complexes, elevated levels of which are associated with numerous disease states, including systemic lupus erythematosus (SLE) and rheumatoid arthritis.

ABSTRACT WORD COUNT: 70

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	805
SPEC A	(English)	EPABF1	6352
Total word count - document A			7157
Total word count - document B			0
Total word count - documents A + B			7157

4/3,AB/25 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00314454
Expression vectors for the production of human Granulocyte-Macrophage Colony Stimulation Factor in a mammalian cell host(18.05.92).
Expressionsvektoren fur die Produktion von humanem GM-CSF in Sangerzellen.
Vecteurs d'expression du GM-CSF humain dans des cellules de mammiferes.
PATENT ASSIGNEE:
Schering Biotech Corporation, (636051), 901 California Avenue, Palo Alto California 94304-1104, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Yokota, Takashi, 890 Colorado Avenue, Palo Alto California 94303, (US)
Lee, Frank D., 212 Rinconada Avenue, Palo Alto California 94301, (US)
Rennick, Donna M., 601 Almond Avenue, Los Altos California 94022, (US)
Arai, Ken-ichi, 648 Georgia Avenue, Palo Alto California 94306, (US)
Arai, Naoko, 648 Georgia Avenue, Palo Alto California 94306, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 299782 A2 890118 (Basic)
EP 299782 A3 890809
EP 299782 B1 930407
APPLICATION (CC, No, Date): EP 88306486 880715;
PRIORITY (CC, No, Date): US 74988 870717
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12P-021/02;

ABSTRACT EP 299782 A2

Human granulocyte-macrophage colony stimulating factor (GM-CSF) polypeptides are provided, as well as methods for synthesizing conformationally and antigenically neutral muteins. The disclosed GM-CSFs promote growth and development of various hematopoietic lineages, and may be useful in treating conditions involving depressed blood cell populations and/or depressed blood cell regeneration, such as myeloid

hypoplasia, chronic infections, and hematopoiesis after bone marrow transplantation. The invention also includes a novel mammalian expression vector.
ABSTRACT WORD COUNT: 73

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	346
CLAIMS B	(German)	EPBBF1	205
CLAIMS B	(French)	EPBBF1	294
SPEC B	(English)	EPBBF1	10375
Total word count - document A			0
Total word count - document B			11220
Total word count - documents A + B			11220

4/3,AB/26 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00309966
Vaccine against pasteurella
Impfstoff gegen Pasteurella
Vaccin contre pasteurella
PATENT ASSIGNEE:
BTG INTERNATIONAL LIMITED (Company No. 2664412), (1475433), 10 Fleet Place Limeburner Lane, London EC4M 7SB, (GB), (Proprietor designated states: all)
INVENTOR:
Donachie, William, 7 Beechbank Crescent, East Calder, West Lothian, EH53 0DX, (GB)
LEGAL REPRESENTATIVE:
Percy, Richard Keith et al (46441), Patents Department British Technology Group Ltd 10 Fleet Place, London EC4M 7SB, (GB)
PATENT (CC, No, Kind, Date): EP 287206 A1 881019 (Basic)
EP 287206 B1 930804
EP 287206 B2 991124
APPLICATION (CC, No, Date): EP 88301932 880304;
PRIORITY (CC, No, Date): GB 8706944 870324; GB 8721286 870910
DESIGNATED STATES: BE; DE; ES; FR; IT; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/02; C12N-001/38; C12P-021/00; C07K-001/00; C07K-001/14

ABSTRACT EP 287206 A1
A vaccine against pasteurellosis is obtained from Pasteurella grown under iron restriction conditions.
ABSTRACT WORD COUNT: 17

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9947	900
CLAIMS B	(German)	9947	934
CLAIMS B	(French)	9947	1005
SPEC B	(English)	9947	6261
Total word count - document A			0
Total word count - document B			9100

Total word count - documents A + B 9100

4/3,AB/27 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00272438
Human pleiotropic immune factor and muteins thereof.
Menschlicher pleitroper Immunfaktor und dessen Muteine.
Facteur immune et pleiotropique humain et des muteines de celui-ci.
PATENT ASSIGNEE:
Schering Biotech Corporation, (636051), 901 California Avenue, Palo Alto California 94304-1104, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Coffman, Robert, 239 Echo Lane, Portola Valley California 94025, (US)
Yokota, Takashi, 890 Colorado Avenue, Palo Alto California 94303, (US)
Crute, James J., 422 College Avenue, Palo Alto California 94306, (US)
Lee, Frank, 212 Rinconada Avenue, Palo Alto California 94301, (US)
Arai, Ken-ichi, 648 Georgia Avenue, Palo Alto California 94306, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al , Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 267779 A2 880518 (Basic)
EP 267779 A3 900117
APPLICATION (CC, No, Date): EP 87309935 871110;
PRIORITY (CC, No, Date): US 928900 861110; US 551 870105
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/02; C07K-013/00; C12N-015/00; A61K-037/02;

ABSTRACT EP 267779 A2
A novel immune system mediator, termed pleiotropic immune factor (PIF) is provided which enhances the secretion of immunoglobulin, particularly IgA, and which promotes the growth and differentiation of eosinophils. The human PIF amino acid sequence is disclosed, and a synthetic gene is provided for cassette mutagenesis in a pcD plasmid. Mutant and native human PIFs are expressed in COS 7 monkey cells.
ABSTRACT WORD COUNT: 66

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1129
SPEC A	(English)	EPABF1	15986
Total word count - document A			17115
Total word count - document B			0
Total word count - documents A + B			17115

4/3,AB/28 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00256827
Preparation of binding factor related polypeptides.
Herstellung von verwandten Polypeptiden des Bindungsfaktors.

Preparation de polypeptides parents a facteur de liaison.
PATENT ASSIGNEE:
CIBA-GEIGY AG, (201300), Klybeckstrasse 141, CH-4002 Basel, (CH),
(applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Hofstetter, Hans, Dr., Wasserstelzenweg 38, CH-4125 Riehen, (CH)
Kilchherr, Erich, Dr., Muligass 3C, CH-5264 Gipf-Oberfrick, (CH)
Schmitz, Albert, Dr., Gasstrasse 53, CH-4056 Basel, (CH)
LEGAL REPRESENTATIVE:
Zumstein, Fritz, Dr. et al (13562), Brauhausstrasse 4, W-8000 Munchen 2, (DE)
PATENT (CC, No, Kind, Date): EP 254249 A1 880127 (Basic)
EP 254249 B1 920819
APPLICATION (CC, No, Date): EP 87110458 870720;
PRIORITY (CC, No, Date): GB 8617862 860722; GB 8626622 861107
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-013/00; C12N-015/00; C12P-021/00; C07H-021/04; C12N-001/20; C12N-005/00; A61K-037/02; C12N-001/20; C12R-001/19; C12N-001/20; C12R-001/865

ABSTRACT EP 254249 A1
the invention concerns polypeptides related to human immunoglobulin E binding factors (IgE-BFs), mRNAs, DNAs and hybrid vectors coding for said polypeptides, host containing said hybrid vectors, process for the preparation of said polypeptides, mRNAs, DNAs, hybrid vectors, and hosts. The polypeptides can be used for the prevention and/or the treatment of allergic diseases, and accordingly the invention concerns also pharmaceutical preparations containing them.
ABSTRACT WORD COUNT: 67

LANGUAGE (Publication,Procedural,Application): English; German; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	3877
CLAIMS B	(German)	EPBBF1	3493
CLAIMS B	(French)	EPBBF1	3894
SPEC B	(English)	EPBBF1	19529
Total word count - document A			0
Total word count - document B			30793
Total word count - documents A + B			30793

4/3,AB/29 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00236260
INTERLEUKIN-4 PROTEIN HAVING BCGF AND TCGF ACTIVITY ON HUMAN CELLS (HUMAN INTERLEUKIN-4)
INTERLEUKIN-4 PROTEIN MIT BCGF- UND TCGF-AKTIVITAT GEGENUBER MENSCHLICHEN ZELLEN (MENSCHLICHES INTERLEUKIN-4)
INTERLEUKINE-4 PROTEINE AYANT UNE ACTIVITE BCGF AND TCGF VERS CELLULES HUMAINES (INTERLEUKINE-4 HUMAINE)
PATENT ASSIGNEE:
Schering Biotech Corporation, (636051), 901 California Avenue, Palo Alto California 94304-1104, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:

LEE, Frank, 212 Rinconada Avenue, Palo Alto, CA 94301, (US)
YOKOTA, Takashi, 890 Colorado Avenue, Palo Alto, CA 94303, (US)
ARAI, Ken-ichi, 648 Georgia Avenue, Palo Alto, CA 94306, (US)
MOSMANN, Timothy, 69 Lloyden Drive, Atherton, CA 94025, (US)
RENNICK, Donna, 601 Almond Avenue, Los Altos, CA 94022, (US)
SMITH, Craig, 350 Franklin Street, Mountain View, CA 94041, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al (35281), Mathys & Squire 100 Grays Inn Road, London WC1X 8AL, (GB)
PATENT (CC, No, Kind, Date): EP 249613 A1 871223 (Basic)
EP 249613 B1 960703
WO 8702990 870521
APPLICATION (CC, No, Date): EP 86907184 861119; WO 86US2464 861119
PRIORITY (CC, No, Date): US 799668 851119; US 799669 851119; US 843958 860325; US 881553 860703; US 908215 860917
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C07K-014/54; C12N-015/70; A61K-038/20;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	3151
CLAIMS B	(German)	EPAB96	3155
CLAIMS B	(French)	EPAB96	3399
SPEC B	(English)	EPAB96	26958
Total word count - document A			0
Total word count - document B			36663
Total word count - documents A + B			36663

4/3,AB/30 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00224049
Mammalian interleukin-4.
Saugetier-Interleukin-4.
Interleukine-4 mammalienne.
PATENT ASSIGNEE:
Schering Biotech Corporation, (636051), 901 California Avenue, Palo Alto California 94304-1104, (US), (applicant designated states: ES;GR)
INVENTOR:
Lee, Frank, 212 Rinconada Avenue, Palo Alto California 94301, (US)
Yokota, Takashi, 890 Colorado Avenue, Palo Alto California 94303, (US)
Arai, Ken-ichi, 638 Georgia Avenue, Palo Alto California 94306, (US)
Mosmann, Timothy, 69 Lloyden Drive, Atherton California 94025, (US)
Rennick, Donna, 601 Almond Avenue, Los Altos California 94022, (US)
Smith, Craig, 350 Franklin Street, Mountain View California 94041, (US)
LEGAL REPRESENTATIVE:
Ritter, Stephen David et al , Mathys & Squire 10 Fleet Street, London EC4Y 1AY, (GB)
PATENT (CC, No, Kind, Date): EP 230107 A1 870729 (Basic)
APPLICATION (CC, No, Date): EP 86309041 861119;
PRIORITY (CC, No, Date): US 799668 851119; US 799669 851119; US 843958 860325; US 881553 860703; US 908215 860917
DESIGNATED STATES: ES; GR
INTERNATIONAL PATENT CLASS: C07K-015/00; C07K-013/00; C12N-015/00;

C12P-021/00; A61K-037/02;

ABSTRACT EP 230107 A1
Mammalian proteins and muteins thereof, designated interleukin-4s (IL-4s), are provided which exhibit both *B"** *cell"** growth factor activity and T cell growth factor activity. Compounds of the invention include native human and murine IL-4s, muteins thereof, and nucleic acids which are effectively homologous to disclosed cDNAs, and/or which are capable of coding for mammalian IL-4s and their muteins.
ABSTRACT WORD COUNT: 62

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1924
SPEC A	(English)	EPABF1	27101
Total word count - document A			29025
Total word count - document B			0
Total word count - documents A + B			29025

4/3,AB/31 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0280666 DBR Accession No.: 2002-04807 PATENT
Use of an *enterobacterium"** *OmpA"** protein for prophylactic and therapeutic treatment of viral, bacterial, fungal and parasitic infections - *Klebsiella"** *pneumoniae"** recombinant *OmpA"** protein preparation useful for gene therapy
AUTHOR: Jeannin P; Delneste Y; Baussant T
CORPORATE SOURCE: Boulogne, France.
PATENT ASSIGNEE: Pierre-Fabre-Med. 2001
PATENT NUMBER: WO 200187326 PATENT DATE: 20011122 WPI ACCESSION NO.: 2002-055641 (200207)
PRIORITY APPLIC. NO.: FR 20006199 APPLIC. DATE: 20000516
NATIONAL APPLIC. NO.: WO 2001FR1490 APPLIC. DATE: 20010516
LANGUAGE: French
ABSTRACT: Use of an *enterobacterium"** *OmpA"** protein, or one of its fragments or protein derivatives to prepare an pharmaceutical composition in which the level of *OmpA"** protein is 0.08 to 1 mM, is new. The *OmpA"** protein is prepared by extraction of a culture of *enterobacterium"**, or by recombinant methods. The *enterobacterium"** is *Klebsiella"** *pneumoniae"**. Protein sequence data is disclosed. The *OmpA"** protein is useful in prophylactic and therapeutic treatment of virus, bacterium, fungus and parasite infections. In an example, human peripheral blood mononucleated cells were purified using a Ficoll slope and further purified by positive selection using a magnetic cell separator. These *monocytes"** were cultured for 5-7 days with 10 ng/ml of granulocyte macrophage colony stimulating factor to 5x100,000 cells per 5 ml well in a 6-well culture plate containing 10% calf fetal serum, 50 U/ml penicillin, 2 mM glutamine, 50 mg/ml streptomycin, 10 mM HEPES buffer and 0.1 mM non-essential amino acids. This gave human microphages. These were incubated with the *OmpA"** protein derived from *Klebsiella"** *pneumoniae"** having sequence SEQ ID No.1 given in the patent. (33pp)

4/3,AB/32 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0274022 DBR Accession No.: 2001-14229 PATENT
Purified solution of recombinant polypeptide for immunization - soluble *Klebsiella"** *pneumoniae"** recombinant P40 *outer"** *membrane"** *protein"**-*A"** preparation and immunization in mouse for recombinant vaccine, vaccine adjuvant and disease therapy
AUTHOR: Baussant T; Jeannin P; Delneste Y; Lawny F; Bonnefoy J Y
CORPORATE SOURCE: France.
PATENT ASSIGNEE: Pierre-Fabre-Med. 2001
PATENT NUMBER: FR 2803302 PATENT DATE: 20010706 WPI ACCESSION NO.: 2001-427232 (2046)
PRIORITY APPLIC. NO.: FR 200070 APPLIC. DATE: 20000104
NATIONAL APPLIC. NO.: FR 200070 APPLIC. DATE: 20000104
LANGUAGE: French
ABSTRACT: Preparation of a purified solution of a recombinant protein (I) that is soluble in aq. solvent in absence of surfactant (II) is new and involves: removing (II); solubilizing (I) in solution of denaturing agent; and eluting, in aq. solution, soluble (I) by molecular sieving column chromatography. Also claimed are: water-soluble (I) produced by the method; modulating the immune system in mammals towards an antigen by inducing maturation of isolated *dendritic"** cells (*DC"**) in the presence of (I); and modulating the immune system in a mammal by injecting (I), alone or as adjuvant. The preferred (I), *outer"** *membrane"** *protein"**-*A"** (P40) of *Klebsiella"** *pneumoniae"**, binds selectively to *antigen"**-presenting *cell"** , so provides targeting, proliferation and/or expression of molecules by these cells. Recombinant soluble P40 was conjugated with ovalbumin and the composition used to inject mice. (I) are used, alone as vaccine or as an adjuvant, to produce therapeutic compositions that are soluble in absence of (II). (I) is useful for treating various disease, especially cancer, virus infections and bacterial infections. (34pp)

4/3,AB/33 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0256038 DBR Accession No.: 2000-10528 PATENT
Use of *enterobacterial"** *outer"** *membrane"** *protein"**-*A"** for delivering active substances, particularly immunogens for treating or preventing e.g. cancer, to *antigen"** presenting *cells"** - protein antigen delivery system for disease therapy and gene therapy
AUTHOR: Bonnefoy J Y; Lecoanet S; Aubry J P; Jeannin P; Baussant T
CORPORATE SOURCE: Boulogne-Billancourt, France.
PATENT ASSIGNEE: Pierre-Fabre-Medi. 2000
PATENT NUMBER: WO 200027432 PATENT DATE: 20000518 WPI ACCESSION NO.: 2000-387342 (2033)
PRIORITY APPLIC. NO.: FR 9814007 APPLIC. DATE: 19981106
NATIONAL APPLIC. NO.: WO 99FR2734 APPLIC. DATE: 19991108
LANGUAGE: French
ABSTRACT: Use of a pharmaceutical composition with an *outer"** *membrane"** *protein"**-*A"** (*Omp"**-*A"**), or its fragments, for specific targeting of an active substance (I) to *antigen"** presenting *cells"** (APC) is new. *OmpA"** is used to deliver an antigen or hapten to modify (specifically to improve) an immune response, especially for

treatment or prevention of cancers, autoimmune disease, cardiovascular or central nervous system diseases, inflammation, infection or immune deficiency. *OmpA"** specifically binds to APCs and is internalized by them. In an example, recombinant P40 (protein from *Klebsiella"** *pneumoniae"** IPI145) was coupled to the fluorophore Alexa488, and the conjugate added at 1 uM to about 0.2 million cells. The cells were incubated for 1 hr at 4 deg, then washed and analyzed by flow cytometry. Specific binding of the conjugate was observed for peripheral blood *monocytes"**, *dendritic"** cells developed from these *monocytes"** and for *B"**-*lymphocytes"**, but cells other than APCs, e.g. T-lymphocytes, did not bind. (I) is a lipopeptide poly- or oligosaccharide, nucleic acid or chemical. The *OmpA"**/(1) product is transferred e.g. a liposome, virus vector, or host cells transfected to express the product. (34pp)

- Author (s)

Set	Items	Description
S5	520	AU=(BONNEFOY, J? OR BONNEFOY J?)
S6	4	AU=(LECOANET, S? OR LECOANET S?)
S7	815	AU=(AURBY, J? OR AURBY J? OR AUBRY, J? OR AUBRY J?)
S8	512	AU=(PASCALE, J? OR PASCALE J? OR JEANNIN, P? OR JEANNIN P?)
S9	87	AU=(BAUSSANT, T? OR BAUSSANT T?)
S10	2	S5 AND S6 AND S7 AND S8 AND S9
S11	201	S5 AND (S6 OR S7 OR S8 OR S9)
S12	4	S6 AND (S7 OR S8 OR S9)
S13	38	S7 AND (S8 OR S9)
S14	11	S8 AND S9
S15	32	(S11 OR S13 OR S5 OR S6 OR S7 OR S8 OR S9) AND (S1 OR S2)
S16	16	(S10 OR S12 OR S14 OR S15) NOT S3
S17	12	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

17/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12317217 References: 27
TITLE: Cutting edge: *Outer"** *membrane"** *protein"** *A"** (*OmpA"**) binds to and activates human macrophages
AUTHOR(S): Soulas C; *Baussant T"**; *Aubry JP"**; Delneste Y; Barillat N; Caron G; Renno T; *Bonnefoy JY"**; *Jeannin P (REPRINT)"**
AUTHOR(S) E-MAIL: pascale.jeannin@pierre-fabre.com
CORPORATE SOURCE: Ctr Immunol Pierre Fabre, 5 Ave Napoleon III/F-74164 St Julien En Genevois//France/ (REPRINT); Ctr Immunol Pierre Fabre, /F-74164 St Julien En Genevois//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF IMMUNOLOGY, 2000, V165, N5 (SEP 1), P2335-2340
GENUINE ARTICLE#: 390MF
PUBLISHER: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA
ISSN: 0022-1767
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Outer membrane protein (*Omp"**)*A"** is highly represented and conserved in the *Enterobacteriaceae"** family. Using a recombinant *OmpA"** From Klehsiella pneumoniae (P40), we have analyzed the interaction between *OmpA"** and macrophages. We report that Alexa(488)-labeled P40 binds (at 4 degreesC) to murine and human macrophages in a dose-dependent manner and is rapidly internalized (at 37 degreesC), No binding or

internalization of the Alexa(488)-labeled glycophorin A control protein is observed under the same conditions, Furthermore, P40 up-regulates the production of IL-1 beta, IL-8, IL-10, IL-12, and TNF-alpha by human macrophages and of NO by the RAW 264.7 murine macrophage cell line, P40 also synergizes with IFN-gamma and suboptimal concentrations of LPS to up-regulate the production of these mediators. In conclusion, P40 binds to and activates macrophages, These data suggest that recognition of *OmpA"** by macrophages may be an initiating event in the antibacterial host response.

17/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09682492 References: 57
TITLE: The recombinant *Klebsiella"** *pneumoniae"** outer membrane protein *OmpA"** has carrier properties for conjugated antigenic peptides
AUTHOR(S): Haeuw JF (REPRINT); Rauly I; Zanna L; Libon C; Andreoni C; Nguyen TN; *Baussant T"**; *Bonnefoy JY"**; Beck A
CORPORATE SOURCE: CTR IMMUNOL PIERRE FABRE,DEPT BIOCHEM, 5 AVE NAPOLEON III, BP 497/F-74164 ST JULIEN EN GENEVOIS//FRANCE/ (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: EUROPEAN JOURNAL OF BIOCHEMISTRY, 1998, V255, N2 (JUL 15), P 446-454
GENUINE ARTICLE#: 102YU
PUBLISHER: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010
ISSN: 0014-2956
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: *Klebsiella"** *pneumoniae"** *OmpA"**, the 40-kDa major protein of the outer membrane, was cloned and expressed in Escherichia coil. The recombinant protein was produced intracellularly in E. coil as inclusion bodies. Fusion of a short peptide to the N-terminus of native P40 facilitated high-level expression of the recombinant protein. Purified recombinant P40 was analyzed to verify purity and structural integrity. The molecular mass of purified recombinant P40 determined by electrospray mass spectrometry was 37061 Da, in agreement with the theoretical mass deduced from the DNA sequence. Specific proliferation of recombinant-P40-primed murine lymph node cells in response to recombinant P40 stimulation ill vitro indicated the presence of a T-cell epitope on recombinant P40. The induction of high serum antibody titers to a synthetic peptide derived from the attachment protein G of the respiratory syncytial virus when chemically coupled to recombinant P40 indicated that the protein had potent carrier properties.

17/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09387561 References: 31
TITLE: Chromosomal sequencing using a PCR-based biotin-capture method allowed isolation of the complete gene for the *outer"** *membrane"** *protein"** *A"** of *Klebsiella"** *pneumoniae"**
AUTHOR(S): Nguyen TN; Samuelson P; Sterky F; MerlePoitte C; Robert A; *Baussant T"**; Haeuw JF; Uhlen M; Binz H; Stahl S (REPRINT)
CORPORATE SOURCE: KUNGLIGA TEKN HGSK,DEPT BIOCHEM & BIOTECHNOL/S-10044

STOCKHOLM//SWEDEN/ (REPRINT); KUNGLIGA TEKN HGSK,DEPT BIOCHEM & BIOTECHNOL/S-10044 STOCKHOLM//SWEDEN/; CTR IMMUNOL PIERRE FABRE,/F-74164 ST JULIEN EN GENEVOIS//FRANCE/
PUBLICATION TYPE: JOURNAL
PUBLICATION: GENE, 1998, V210, N1 (MAR 27), P93-101
GENUINE ARTICLE#: ZH126
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
ISSN: 0378-1119
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: By employing a novel biotin-and PCR-assisted capture method, which allows determination of unknown sequences on chromosomal DNA. the gene for the *outer"** *membrane"** *protein"** *A"** (*OmpA"**) of *Klebsiella"** *pneumoniae"** has been isolated and sequenced to completion. The method involves linear amplification of DNA from a biotinylated primer annealing to a region with known sequence. After capture of the amplified single-stranded DNA on to paramagnetic beads, unspecifically annealing primers, i.e. arbitrary primers, were used to generate fragments with only partly determined nt sequences. The homology of the sequenced gene to ompAs of related bacteria is discussed. The *ompA"** gene was assembled for intracellular expression in Escherichia coli, and two different fusion proteins were produced and recovered with good yields. The importance of the novel chromosomal sequencing method for gene isolation in general and the potential use of the *OmpA"** fusion proteins are discussed. (C) 1998 Elsevier Science B.V.

17/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09328807 References: 44
TITLE: IgE versus IgG4 production can be differentially regulated by IL-10
AUTHOR(S): *Jeannin P (REPRINT)"**; *Lecoanet S"**; Delneste Y; Gauchat JF; Bonnefoy JY
CORPORATE SOURCE: CTR IMMUNOL PIERRE FABRE,5 AVE NAPOLEON 3, BP 97/F-74164 ST JULIEN EN GENEVOIS//FRANCE/ (REPRINT); GLAXO WELLCOME RES & DEV SA,DEPT IMMUNOL, GENEVA BIOMED RES INST/GENEVA//SWITZERLAND/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1998, V160, N7 (APR 1), P3555-3561
GENUINE ARTICLE#: ZD573
PUBLISHER: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814
ISSN: 0022-1767
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Allergen-specific IgE plays a key role in the physiopathology of allergic disorders, This IgE response is usually accompanied by a production of IgG4, Indirect evidence suggests that IgG4 may not be a sensitizing Ab but, in contrast, could be protective, As such, it may be of potential therapeutic interest to selectively modulate IgE vs IgG4 production, To date, IgE and IgG4 switching seems to be controlled by common mechanisms, We report here that IL-10 has a differential effect on IgE vs IgG4 production by PBMC, IL-10 decreases epsilon transcript expression and IgE production induced by IL-4 when added during the first 3 days of in vitro culture, suggesting that IL-10 decreases IL-4-induced IgE switching, In contrast, if added later on B cells that are already IgE switched, IL-10 potentiates IgE production, Interestingly, whatever the

time of addition, IL-10 augments IL-4-induced gamma 4 transcript expression and IgG4 production, with a maximal effect when added during the first 3 days, As IL-10 is not a switch factor for IgG4, it is likely that IL-10 enhances IgG4 production by potentiating IL-4-induced IgG4 switching. However, IL-10 may also act by enhancing the growth and/or differentiation of cells that are already IgG4 committed, Finally, CD40 ligation reverses the early down-regulating effect of IL-10 on IgE production. These results are the first evidence of a molecule that differentially regulates IgE vs IgG4 production, thereby suggesting the existence of a pathway(s) selectively controlling their production.

17/3,AB/5 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01381767
USE OF AN *ENTEROBACTERIUM"** *OMPA"** PROTEIN AS ANTIMICROBIAL AGENT
VERWENDUNG VON EINEM BAKTERIELLE *OMPA"** PROTEINE ALS ANTIMIKROBIELLES VERMITTEL
UTILISATION D'UNE PROTEINE *OmpA"** D'*ENTEROBACTERIE"** COMME AGENT ANTIMICROBIEN
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)
INVENTOR:
*JEANNIN, Pascale"**, 8, allee des Cedres, F-74160 Saint-Julien-en-Genevois, (FR)
DELNESTE, Yves, 8, allee des Cedres, F-74160 Saint-Julien-en-Genevois, (FR)
*BAUSSANT, Thierry"**, 4, rue Alphonse Baudin, F-01200 Bellegarde, (FR
PATENT (CC, No, Kind, Date): WO 2001087326 011122
APPLICATION (CC, No, Date): EP 2001936538 010516; WO 2001FR1490 010516
PRIORITY (CC, No, Date): FR 006199 000516
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-038/16; A61K-039/39
LANGUAGE (Publication,Procedural,Application): French; French; French

17/3,AB/6 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01325109
METHOD FOR PREPARING A POLYPEPTIDE SOLUBLE IN AN AQUEOUS SOLVENT IN THE ABSENCE OF DETERGENT
VERFHAREN ZUR HERSTELLUNG EINES IM WASSRIGEN LOSUNGSMITTEL IN ABWESENHEIT VON DETERGENTIEN LOSLICHEN POLYPEPTIDS
PROCEDE DE PREPARATION D'UN POLYPEPTIDE SOLUBLE EN SOLVANT AQUEUX EN ABSENCE DE DETERGENT
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)
INVENTOR:
*BAUSSANT, Thierry"**, 4, rue Alphonse Baudin, F-01200 Bellegarde, (FR)

*JEANNIN, Pascale"**, 8, allee des Cedres, F-74160 Saint-Julien-en-Genevois, (FR)
DELNESTE, Yves, 8, allee des Cedres, F-74160 Saint-Julien-en-Genevois, (FR)
LAWNY, Francois, 19, rue des Champs de Chant, F-74800 Saint-Sixt, (FR)
BONNEFOY, Jean-Yves, Les Noyers, F-74350 Le Sappey, (FR
LEGAL REPRESENTATIVE:
Warcoin, Jacques (19071), Cabinet Regimbeau 20, rue de Chazelles, 75847 Paris cedex 17, (FR)
PATENT (CC, No, Kind, Date): EP 1244690 A2 021002 (Basic)
WO 2001049705 010712
APPLICATION (CC, No, Date): EP 2001903868 010104; WO 2001FR23 010104
PRIORITY (CC, No, Date): FR 0070 000104
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C07K-001/34; C07K-014/26; C07K-014/205
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): French; French; French

17/3,AB/7 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01294512
Peptide fragment of the respiratory syncytial virus g protein, immunogenic agent, pharmaceutical composition containing same , and preparation method
Peptidfragmente des g-proteins des respiratorischen syncytialvirus, immunogene verbindung und pharmazeutische zusammensetzung, die es enthaelt, und herstellungsverfahren
Fragment peptidique de la proteine g du virus respiratoire syncytial, agent immunogene, composition pharmaceutique le contentant et procede de preparation
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629912), 45, Place Abel Gance, 92100 Boulogne, (FR), (Applicant designated States: all)
INVENTOR:
Binz, Hans, Haldenweg 1, 4533 Riedholz, (CH)
N Guyen Ngoc, Thien, 7 Les Petits Hutins, Lathoy, 74160 Saint-Julien-en-Genevois, (FR)
*Baussant, Thierry"**, 4 rue Alphonse Baudin, 01200 Bellegarde, (FR)
Trudel, Michel, 88 Val d'Ajol, Lorraine, Quebec J6Z 3Y3, (CA
LEGAL REPRESENTATIVE:
Warcoin, Jacques et al (19071), Cabinet Regimbeau 20, rue de Chazelles, 75847 Paris cedex 17, (FR)
PATENT (CC, No, Kind, Date): EP 1111053 A2 010627 (Basic)
EP 1111053 A3 010808
APPLICATION (CC, No, Date): EP 2000126606 950406;
PRIORITY (CC, No, Date): FR 944009 940406
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 754231 (EP 95916721)
INTERNATIONAL PATENT CLASS: C12N-015/45; C12N-015/31; C07K-014/135; C07K-014/26; C07K-014/765; A61K-039/155; A61K-047/48

ABSTRACT EP 1111053 A2 (Translated)

New respiratory syncytial virus polypeptide(s) for vaccine prodn.

New polypeptides (I) useful as immunogenic elements comprise a peptide sequence between amino acids 130 and 230 of the protein G sequence of respiratory syncytial virus (RSV) subgroup A or B, or a sequence having at least 80% homology with this sequence. Also claimed are: (1) an immunogenic agent comprising a polypeptide (I) coupled to a carrier protein; (2) a compsn. for preventing and/or treating RSV subgroup A and/or B infections contg. a polypeptide (I) or an immunogenic agent as in (1); (3) a nucleotide sequence coding for a polypeptide (I); (4) a protein (namely *Klebsiella"** *pneumoniae"** p40 protein) with a defined sequence of 335 amino acids given in the specification, or with 80% homology with this sequence; (5) a nucleotide sequence coding for *K"**. *pneumoniae"** p40 protein; and (6) a process for preparing a peptide conjugate for use in the compsn. of (2).

TRANSLATED ABSTRACT WORD COUNT: 151

ABSTRACT EP 1111053 A2

La presente invention concerne un polypeptide utilisable comme element d'immunogene, caracterise en ce qu'il est porte par la sequence peptidique comprise entre les residus d'acides amines 130 et 230 de la sequence de la proteine G du virus respiratoire syncytial humain du sous-groupe A et du sous-groupe B, ou du virus respiratoire syncytial bovin, ou par une sequence presentant au moins 80% d'homologie avec ladite sequence peptidique.

L'invention concerne egalement un agent immunogene ou une composition pharmaceutique contenant le polypeptide et leur procede de preparation.

ABSTRACT WORD COUNT: 86

NOTE:

Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): French; French; French

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(French)	200126	834
SPEC A	(French)	200126	6193
Total word count - document A			7027
Total word count - document B			0
Total word count - documents A + B			7027

17/3,AB/8 (Item 4 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

01204193

PROTEIN *OmpA"** OF $i(*KLEBSIELLA"** *PNEUMONIAE"**) ASSOCIATED WITH THE HCG HORMONE OR A COMPOUND INVOLVED IN CELL PROLIFERATION OR FERTILITY

PROTEIN *OMPA"** AUS *KLEBSIELLA"** *PNEUMONIAE"** ASSOZIERT MIT DEM HCG HORMON ODER MIT EINER ZUSAMMENSETZUNG, WELCHE AN DEN PROLIFERATION VON TUMORZELLEN ODER AN DER FERTILITAT BETEILIGT IST

PROTEINE *OMPA"** DE *KLEBSIELLA"** *PNEUMONIAE"** ASSOCIEE A L'HORMONE HCG OU A UN COMPOSE IMPLIQUE DANS LA PROLIFERATION DE CELLULES TUMORALES OU DANS LA FERTILITE

PATENT ASSIGNEE:

PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)

INVENTOR:
GOETSCH, Liliane, Route de Bonneville, 74130 Ayze, (FR)
CORVAIA, Nathalie, Res. "Les Chenes", 32, rue des Chenes, 74160 St. Julien en Genevois, (FR)
BECK, Alain, 503, route du Poirier a l'Ane, 74160 Collonges sous Saleve, (FR)
HAEUW, Jean-Francois, Les Jardins de l'Atrium, 8, av. de Ternier, 74160 St. Julien en Genevois, (FR)
*BONNEFOY, Jean-Yves"**, Les Noyers, F-74350 Le Sappey, (FR
PATENT (CC, No, Kind, Date): WO 200050071 000831
APPLICATION (CC, No, Date): EP 2000907716 000224; WO 2000FR463 000224
PRIORITY (CC, No, Date): FR 992314 990224
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/00; A61K-039/385; A61K-048/00; A61K-039/39; A61P-035/00; A61P-037/04; C07K-014/26; C07K-14:59; C07K-14:34
LANGUAGE (Publication,Procedural,Application): French; French; French

17/3,AB/9 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01201915
USE OF AN *OmpA"** *ENTEROBACTERIUM"** PROTEIN ASSOCIATED WITH THE ELAGIGILTV PEPTIDE FOR TREATING MELANOMAS
VERWENDUNG DES PROTEINS *OMPA"** AUS ENTEROBAKTERIEN ASSOZIERT MIT PEPTID ELAGIGILTV ZUR BEHANDLUNG DER MELANOMEN
UTILISATION D'UNE PROTEINE *OmpA"** D'*ENTEROBACTERIE"** ASSOCIEE AU PEPTIDE ELAGIGILTV POUR LE TRAITEMENT DES MELANOMES
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)
INVENTOR:
RENNO, Toufic, Les Coulerins B1, F-74580 Viry, (FR)
ROMERO, Pedro, chemin du Polny 1, CH-1066 Epalinges, (CH)
MICONNET, Isabelle, chemin de Chandolin 5, CH-1005 Lausanne, (CH)
CAROTTINI, Jean-Charles, avenue du Leman 12, CH-1025 Saint-Suplice, (CH)
*BONNEFOY, Jean-Yves"**, Les Noyers, F-74350 Le Sappey, (FR
LEGAL REPRESENTATIVE:
Texier, Christian (53261), Cabinet Regimbeau 20, rue de Chazelles, 75847 Paris cedex 17, (FR)
PATENT (CC, No, Kind, Date): EP 1150707 A1 011107 (Basic)
WO 200048629 000824
APPLICATION (CC, No, Date): EP 2000906412 000217; WO 2000FR394 000217
PRIORITY (CC, No, Date): FR 991917 990217
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/00; A61K-039/385; A61K-048/00; A61P-035/00; C07K-14:26
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): French; French; French

17/3,AB/10 (Item 6 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

01201914
USE OF AN *ENTEROBACTERIUM"** PROTEIN *OMPA"** ASSOCIATED WITH AN ANTIGEN FOR GENERATING AN ANTIVIRAL, ANTIPARASITIC OR ANTITUMORAL CYTOTOXIC RESPONSE
VERWENDUNG DES PROTEINS *OMPA"** AUS ENTEROBAKTERIEN ASSOZIERT MIT EINEM ANTIGEN ZUR ERZEUGUNG EINER ZYTOTOXISCHEN ANTWORT GEGEN VIREN, PARASITEN ODER TUMOREN
UTILISATION D'UNE PROTEINE *OmpA"** D'*ENTEROBACTERIE"** ASSOCIEE A UN ANTIGENE POUR GENERER UNE REPONSE CYTOTOXIQUE ANTIVIRALE, ANTIPARASITAIRE OU ANTITUMORALE
PATENT ASSIGNEE:
PIERRE FABRE MEDICAMENT, (629914), 45, Place Abel Gance, 92100 Boulogne-Billancourt, (FR), (Applicant designated States: all)
INVENTOR:
RENNO, Toufic, Les Coulerins B1, F-74580 Viry, (FR)
*BONNEFOY, Jean-Yves"**, Les Noyers, F-74350 Le Sappey, (FR
LEGAL REPRESENTATIVE:
Ahner, Francis et al (13601), Cabinet Regimbeau 20, rue de Chazelles, 75847 Paris cedex 17, (FR)
PATENT (CC, No, Kind, Date): EP 1150706 A1 011107 (Basic)
WO 200048628 000824
APPLICATION (CC, No, Date): EP 2000906411 000217; WO 2000FR393 000217
PRIORITY (CC, No, Date): FR 991917 990217
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/00; A61K-048/00; A61P-031/00; A61P-033/00; A61P-035/00; A61K-039/385; C07K-014/26; C12N-15:62
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): French; French; French

17/3,AB/11 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0312898 DBR Accession No.: 2003-14038 PATENT
Composition containing peptide from low molecular weight outer membrane protein, useful for preparing vaccines against infections or cancer - recombinant vaccine and nucleic acid vaccine preparation useful for virus infection, bacterium infection and cancer gene therapy
AUTHOR: *JEANNIN P"**; LIBON C; *BAUSSANT T"**; HAEUW J F; GAUCHAT J F
PATENT ASSIGNEE: FABRE MEDICAMENT SA PIERRE 2003
PATENT NUMBER: FR 2828106 PATENT DATE: 20030207 WPI ACCESSION NO.: 2003-335312 (200332)
PRIORITY APPLIC. NO.: FR 200110381 APPLIC. DATE: 20010802
NATIONAL APPLIC. NO.: FR 200110381 APPLIC. DATE: 20010802
LANGUAGE: French
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Pharmaceutical composition containing at least one peptide (I) derived from a low molecular weight outer membrane protein (Omp) from an enterobacterium, or the nucleic acid that encodes (I), is new. ACTIVITY - Virucide; Antibacterial; Fungicide; Antiparasitic; Cytostatic. No biological data is given. MECHANISM OF ACTION - Vaccine. USE - The compositions are used, by combining with an antigen, immunogen or hapten from a pathogen (viral,

bacterial, fungal or parasite) or tumor cells, to make vaccines for treatment or prevention of infections or cancer, especially infection by respiratory syncytial virus. (I) functions as carrier and/or adjuvant. ADVANTAGE - (I) increases the immunogenicity of antigens etc. combined with it. EXAMPLE - The 170 amino acid outer membrane protein (Omp K17) of Klebsiella pneumoniae was expressed recombinantly then linked (via glutaraldehyde) to angiotensin II (AII). The product (15 micro-g) was administered subcutaneously to mice (days 0, 7 and 14), and periodically the blood titer of anti-AII immunoglobulin determined by enzyme-linked immunosorbent assay. The titer (expressed as optical density) was about 4 on days 21 and 28, and still about 3.7 on day 42. When the same dose of unconjugated AII was administered with Freund's adjuvant the maximum titer was 2.1 on day 28.(39 pages)

17/3,AB/12 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0259160 DBR Accession No.: 2000-13650 PATENT
Use of *enterobacterial"** *outer"** *membrane"** *protein"**-*A"** in vaccines for inducing cytotoxic T-cell responses, useful for treating or preventing infections and tumors - recombinant vaccine and nucleic acid vaccine
AUTHOR: Renno T; *Bonnefoy J Y"**
CORPORATE SOURCE: Boulogne-Billancourt, France.
PATENT ASSIGNEE: Pierre-Fabre-Medicament 2000
PATENT NUMBER: WO 200048628 PATENT DATE: 20000824 WPI ACCESSION NO.: 2000-543667 (2049)
PRIORITY APPLIC. NO.: FR 991917 APPLIC. DATE: 19990217
NATIONAL APPLIC. NO.: WO 2000FR393 APPLIC. DATE: 20000217
LANGUAGE: French
ABSTRACT: Use of an *enterobacterial"** *outer"** *membrane"** *protein"**-*A"** (I) or its fragments for preparing a composition that induces, or increases the cytotoxic T-lymphocyte response against an infectious agent or tumor cell is claimed. Also claimed is a composition of at least one (I) or its fragment mixed with or coupled to at least one antigen or hapten associated with or specific to a tumor cell. (I) or the nucleic acid encoding it are used in recombinant vaccines and nucleic acid vaccines formulation for prevention of infections caused by viruses, bacteria, fungi and parasites or tumors, especially melanoma. (I)-containing compositions induce a cytotoxic T-lymphocyte response without requiring an adjuvant. (44pp)
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07aug03 11:45:44 User219783 Session D1955.2

Devi, S.
09/831061

-key terms

(FILE 'HCAPLUS' ENTERED AT 12:14:14 ON 07 AUG 2003)
L1 69 SEA FILE=HCAPLUS ABB=ON PLU=ON (ENTEROBACTER? OR ENTERO BACTER? OR (KLEBSIEL? OR K)(W)PNEUMON?) AND (OMPA OR (OMP OR OUTER MEMBRAN? PROTEIN)(W)A)
L2 6 SEA FILE=HCAPLUS ABB=ON PLU=ON KPOMPA OR KP(W)(OMPA OR (OMP OR OUTER MEMBRAN? PROTEIN)(W)A)
L3 11 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2) AND (ANTIGEN(1W)CELL OR DENDRIT## OR MONOCYT? OR B(W)(CELL OR LYMPHOCYTE) OR DC(S)DENDRIT##)

L3 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:515586 HCAPLUS
TITLE: **Outer membrane protein A (OmpA)** activates human epidermal Langerhans cells
AUTHOR(S): Godefroy, Sylvie; Corvaia, Nathalie; Schmitt, Daniel; Aubry, Jean-Pierre; Bonnefoy, Jean-Yves; Jeannin, Pascale; Staquet, Marie-Jeanne
CORPORATE SOURCE: Hopital E. Herriot, INSERM U346, affilie CNRS, Lyon, Fr.
SOURCE: European Journal of Cell Biology (2003), 82(4), 193-200
CODEN: EJCBDN; ISSN: 0171-9335
PUBLISHER: Urban & Fischer Verlag GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Outer membrane protein (**Omp**)**A** is highly represented and conserved in the **Enterobacteriaceae** family. Using a recombinant **OmpA** from **Klebsiella pneumoniae** (**kpOmpA**), we have analyzed the interaction between this bacterial cell wall protein and human Langerhans cells (LC), the **antigen**-presenting **cells** of the epidermis and mucosa. We showed that biotinylated **kpOmpA** binds to human LC freshly isolated from epidermis. **KpOmpA** up-regulated MHC class II, CD86 and CCR7 expression, enhanced migration in response to macrophage inflammatory protein-3.beta. (MIP-3.beta.) through a reconstituted basement membrane mimicking the prerequisite passage through the dermal-epidermal basement membrane on the way to lymph nodes. The allostimulatory function of **kpOmpA**-treated LC was more potent than that of untreated cells. Even though the proportion of LC which binds **kpOmpA** was shown to vary between individuals, our data indicate that **kpOmpA** binds to and activates LC, and suggest that recognition of **OmpA** by LC may be an initiating event in the antibacterial host response.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:137763 HCAPLUS
DOCUMENT NUMBER: 138:186095
TITLE: **Outer membrane protein A** renders **dendritic** cells and macrophages responsive to CCL21 and triggers **dendritic** cell migration to secondary lymphoid organs

AUTHOR(S): Jeannin, Pascale; Magistrelli, Giovanni; Herbault, Nathalie; Goetsch, Liliane; Godefroy, Sylvie; Charbonnier, Peggy; Gonzalez, Alexandra; Delneste, Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, Fr.
SOURCE: European Journal of Immunology (2003), 33(2), 326-333
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Outer membrane protein A** (**OmpA**) is a class of bacterial cell wall protein that is immunogenic without adjuvant. As specific immune responses are initiated in the lymph nodes (LN), the authors analyzed the effect of the **OmpA** from **Klebsiella pneumoniae** (**KpOmpA**) on chemokine/chemokine receptor expression by APC and on cell migration to the LN. Upon contact with **KpOmpA** , human immature DC and macrophages acquire CCR7 expression and responsiveness to CCL21. In parallel, CCR1 and CCR5 expression is down-regulated and CXCL8, CCL2, CCL3 and CCL5 prodn. is up-regulated. Mice injected s.c. with **KpOmpA** present a transient inflammatory reaction at the site of injection accompanied by an enlargement of the draining LN with a higher proportion of DC and macrophages. Lastly, when exposed to **KpOmpA** prior injection, DC but not macrophages migrate to the draining LN. In conclusion, **KpOmpA** confers a migratory phenotype to DC and triggers their migration to the regional LN. This property contributes to explain how innate cells initiate adaptive immune response upon recognition of conserved bacterial components and also why **OmpA** is immunogenic in the absence of adjuvant.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:930988 HCAPLUS
DOCUMENT NUMBER: 138:185779
TITLE: **Outer membrane protein A (OmpA)**: a new pathogen-associated molecular pattern that interacts with **antigen** presenting **cells**-impact on vaccine strategies
AUTHOR(S): Jeannin, Pascale; Magistrelli, Giovanni; Goetsch, Liliane; Haeuw, Jean-Francois; Thieblemont, Nathalie; Bonnefoy, Jean-Yves; Delneste, Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.
SOURCE: Vaccine (2002), 20(Suppl. 4), A23-A27
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. **Outer membrane protein A (OmpA)** is a class of proteins highly conserved among the **Enterobacteriaceae** family and throughout

evolution. The authors have obsd. that **antigen** presenting **cells** (APCs) recognize and are activated by the recombinant **OmpA** from **Klebsiella pneumoniae** (**KpOmpA**). **KpOmpA** triggers cytokine prodn. by macrophages and **dendritic** cells (**DC**), induces **DC** maturation and signals via Toll-like receptor 2. **KpOmpA** also interacts with endocytic receptor(s) expressed on DC and macrophages. Tumor antigens coupled to **KpOmpA** are taken up by APCs and gain access to the MHC class I pathway, triggering the initiation of protective anti-tumor cytotoxic responses in the absence of CD4 T cell help and adjuvant. Thus, **OmpA** appears as a new type of pathogen-assocd. mol. pattern (PAMP) usable as a vector in anti-infectious and therapeutic anti-tumor vaccines to elicit CTLs.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:357107 HCAPLUS
DOCUMENT NUMBER: 137:293167
TITLE: Streptococcus pneumoniae polysaccharides conjugated to the **outer membrane protein A** from **Klebsiella pneumoniae** elicit protective antibodies
AUTHOR(S): Libon, Christine; Haeuw, Jean Francois; Crouzet, Francoise; Mugnier, Chantal; Bonnefoy, Jean Yves; Beck, Alain; Corvaia, Nathalie
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, St. Julien en Genevois, 74164, Fr.
SOURCE: Vaccine (2002), 20(17-18), 2174-2180
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polysaccharides (PSs) derived from S. pneumoniae include >90 serotypes and differ greatly in their immunogenicity. In addn., immunization with PSs does not induce high affinity antibody prodn. and no memory **B-cells** are generated. Coupling PSs to carrier proteins has been reported to induce **B-cell** maturation and to install a **B-cell** memory. As an alternative carrier protein, the **outer membrane protein A** (**OmpA**) derived from **K. pneumoniae** has been coupled to various PSs. The authors evaluated the immunogenicity of 2 PS conjugates, using PS derived from S. pneumoniae types 14 and 19, resp. Here, they show that anti-PS IgG responses are generated after the conjugation of PSs to P40. In addn., the humoral response generated is able to protect mice from a bacterial challenge. Thus, P40 could be included in the development of new PS conjugate vaccines.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:127710 HCAPLUS

DOCUMENT NUMBER: 137:61733
TITLE: Stability and CTL-activity of P40/ELA melanoma vaccine candidate
AUTHOR(S): Beck, A.; Goetsch, L.; Champion, T.; Bussat, M.-C.; Aubry, J.-P.; Klinguer-Hamour, C.; Haeuw, J.-F.; Bonnefoy, J.-Y.; Corvaia, N.
CORPORATE SOURCE: BioMerieux-Pierre Fabre, Centre d'Immunologie Pierre Fabre (CIPF), Saint-Julien-en-Genevois, F-74164, Fr.
SOURCE: Biologicals (2001), 29(3/4), 293-298
CODEN: BILSEC; ISSN: 1045-1056
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The decapeptide ELA (ELAGIGILTV), a Melan-A/MART-1 antigen immunodominant peptide analog, is an interesting melanoma vaccine candidate alone or in combination with other tumor antigens. P40, the recombinant **outer membrane protein A** of **Klebsiella pneumoniae** (**kpOmpA**), was recently shown to target **dendritic** cells and to induce peptide-specific CTLs. Here the authors investigated the adjuvant role of P40 mixed or chem. conjugated to ELA. This compd. is an N-terminal glutamic acid-contg. peptide. However, it has been reported that the amino group and the .gamma.-carboxylic group of glutamic acids easily condense to form pyroglutamic derivs. Usually, to overcome this stability problem, peptides of pharmaceutical interest were developed with a pyroglutamic acid instead of N-terminal glutamic acid, without loss of pharmacol. properties. Unfortunately, the pyroglutamic acid deriv. (PyrELA) as well as the N-terminal acetyl capped deriv. (AcELA) failed to elicit CTL activity when mixed with P40 adjuvant protein. Despite the apparent minor modifications introduced by PyrELA and AcELA, these two derivs. have probably lower affinity than ELA for the class 1 Major Histocompatibility Complex. Furthermore, this stability problem is worse in the case of clin. grade ELA, produced as an acetate salt, like most of the pharmaceutical grade peptides. The authors report here that the hydrochloride shows a higher stability than the acetate and may be suitable for use in man. (c) 2001 The International Association of Biological Standardization.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:714059 HCAPLUS
DOCUMENT NUMBER: 136:18965
TITLE: Targeting of nasal mucosa-associated **antigen**-presenting **cells** in vivo with an **outer membrane protein A** derived from **Klebsiella pneumoniae**
AUTHOR(S): Goetsch, Liliane; Gonzalez, Alexandra; Plotnicky-Gilquin, Helene; Haeuw, Jean Francois; Aubry, Jean Pierre; Beck, Alain; Bonnefoy, Jean Yves; Corvaia, Nathalie
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, 74164, Fr.

SOURCE: Infection and Immunity (2001), 69(10), 6434-6444
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Administration of vaccines by the nasal route has recently proven to be one of the most efficient ways for inducing both mucosal and systemic antibody responses in exptl. animals. Our results demonstrate that P40, a well-defined **outer membrane protein A** from **Klebsiella pneumoniae**, is indeed a carrier mol. suitable for nasal immunization. Using fragments from the respiratory syncytial virus subgroup A (RSV-A) G protein as antigen models, it has been shown that P40 is able to induce both systemic and mucosal immunity when fused or coupled to a protein or a peptide and administered intranasally (i.n.) to naive or **K. pneumoniae**-primed mice. Confocal analyses of nasal mucosa-assocd. lymphoid tissue after i.n. instillation of P40 showed that this mol. is able to cross the nasal epithelium and target CD11c-pos. cells likely to be murine **dendritic** cells or macrophages. More importantly, this targeting of **antigen**-presenting **cells** following i.n. immunization with a subunit of the RSV-A mol. in the absence of any mucosal adjuvant results in both upper and lower respiratory tract protection against RSV-A infection.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:590378 HCAPLUS
DOCUMENT NUMBER: 135:302402
TITLE: DC targeting by a bacterial **OmpA**
AUTHOR(S): Blacklaws, Barbara
CORPORATE SOURCE: UK
SOURCE: Trends in Microbiology (2001), 9(4), 159
CODEN: TRMIEA; ISSN: 0966-842X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with one ref., describes a study by Jeannin et al. (2000) involving the use of a bacterial outer membrane protein from **Klebsiella pneumoniae** (**kpOmpA**) to target antigen to the major histocompatibility (MHC) class I compartment of **dendritic** cells. Jeannin et al. isolated recombinant **kpOmpA** and showed it binds to DCs and macrophages, and is internalized by immature DCs and macrophage via receptor-mediated endocytosis. This resulted in maturation of DCs and cytokine receptor. Protein antigens were coupled to **kpOmpA** and found that the coupled antigens are presented to T cells by DCs on MHC class I in a transporter assocd. with antigen processing-dependent manner.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:507718 HCAPLUS

DOCUMENT NUMBER: 135:106360
TITLE: Solubilization of proteins for antigen use in an aqueous solvent without using detergents
INVENTOR(S): Baussant, Thierry; Jeannin, Pascale; Delneste, Yves; Lawny, Francois; Bonnefoy, Jean-Yves
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049705	A2	20010712	WO 2001-FR23	20010104
WO 2001049705	A3	20020214		
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
FR 2803302	A1	20010706	FR 2000-70	20000104
EP 1244690	A2	20021002	EP 2001-903868	20010104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001007421	A	20021022	BR 2001-7421	20010104
JP 2003519238	T2	20030617	JP 2001-550245	20010104
US 2003044915	A1	20030306	US 2002-169953	20020703

PRIORITY APPLN. INFO.: FR 2000-70 A 20000104
WO 2001-FR23 W 20010104

AB The invention concerns a novel method for prepg. a polypeptide sol. in an aq. solvent in the absence of detergent, and polypeptides obtainable by said method. The invention also concerns the use of said polypeptides, in particular for prepg. medicines or vaccines, against bacterial and viral infections or cancers. Specifically, the method is used for hydrophobic membrane proteins such as porins to allow them to be used in vaccines without the use of detergents. The **ompA** porin (rP40) of **Klebsiella pneumoniae** was manufd. by expression of the cloned gene in EScherichia coli where it accumulated as inclusion bodies. The inclusion bodies were recovered from lysates by centrifugation and solubilized in urea 7M, dithiothreitol 10 mM, Tris HCl (25 mM, pH 8.5) at 37.degree. for 2h. The solubilized material was dild. with 13 vols. of NaCl (8.76 g/L), Zwittergent 3-14 (0.1 vol%), Tris HCl (25 mM, pH 8.5) and allowed to renature overnight at room temp. and desalted by dialysis against Tris HCl (25 mM, pH 8.5), Zwittergent 3-14 (0.1 vol%) at 4.degree.. The dialyzed material was purified by ion-exchange chromatog. against strong anion and cation exchangers to yield a protein solubilized with Zwittergent 3-14. The purified protein was pptd. with 5 vols. of ethanol, resolubilized in urea 7M as before to yield a stable hydrophilic form that was predominantly .alpha.-helical as opposed to the hydrophilic .beta.-sheet protein. The protein was able to induce CD38 synthesis and interleukin 12 secretion in human **dendritic** cells. The effects were polymyxin B sensitive and therefore not due to contaminating endotoxins.

L3 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:878892 HCAPLUS

DOCUMENT NUMBER: 134:146071
TITLE: **OmpA** targets **dendritic** cells, induces their maturation and delivers antigen into the MHC class I presentation pathway
AUTHOR(S): Jeannin, Pascale; Renno, Toufic; Goetsch, Liliane; Miconnet, Isabelle; Aubry, Jean-Pierre; Delneste, Yves; Herbault, Nathalie; Baussant, Thierry; Magistrelli, Giovanni; Soulas, Caroline; Romero, Pedro; Cerottini, Jean-Charles; Bonnefoy, Jean-Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.
SOURCE: Nature Immunology (2000), 1(6), 502-509
CODEN: NIAMCZ; ISSN: 1529-2908
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors analyzed the interaction between a bacterial cell wall protein and **dendritic** cells (**DCs**). **Outer membrane protein A** from **Klebsiella pneumoniae** (**kpOmpA**) specifically bound to professional **antigen** presenting **cells** and was endocytosed by immature DCs via a receptor-dependent mechanism. **KpOmpA** signaled through Toll-like receptor 2, induced DCs to produce interleukin 12 and induced maturation of DCs. Whole antigen that was coupled to **kpOmpA** and injected into mice was taken up by DCs and delivered to the conventional cytosolic MHC class I presentation pathway. **KpOmpA** also primed antigen-specific CD8+ CTLs in the absence of CD4+ T cell help or adjuvant and elicited therapeutic immunity to antigen-expressing tumors. Thus, **OmpA** belongs to a class of proteins that are able to elicit CTL responses to exogenous antigen.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:335272 HCAPLUS
DOCUMENT NUMBER: 132:352759
TITLE: Use of an **OmpA** outer membrane protein of an **enterobacterium** for specific targeting of drugs to **antigen** -presenting **cells**
INVENTOR(S): Bonnefoy, Jean-Yves; Lecoanet, Sybille; Aubry, Jean-Pierre; Jeannin, Pascale; Baussant, Thierry
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027432	A1	20000518	WO 1999-FR2734	19991108

W: AU, BR, CA, CN, JP, MX, US, ZA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

FR 2785542	A1	20000512	FR 1998-14007		19981106
FR 2785542	B1	20010209			
BR 9915071	A	20010717	BR 1999-15071		19991108
EP 1124577	A1	20010822	EP 1999-971719		19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002529428	T2	20020910	JP 2000-580661		19991108
PRIORITY APPLN. INFO.:			FR 1998-14007	A	19981106
			WO 1999-FR2734	W	19991108

AB The invention concerns the use of an **enterobacterium** protein **OmpA**, preferably **Klebsiella pneumoniae** P40 protein, for specific targeting of a biol. active substance assocd. therewith towards **antigen** -presenting **cells**, in particular human **dendritic** cells. The invention also concerns the use of the **OmpA** protein for prepg. a pharmaceutical compn. for preventing and/or treating diseases, in particular cancers related to a tumor-assocd. antigen, autoimmune diseases or infectious diseases. The protein can be manufd. as inclusion bodies in Escherichia coli and purified chromatog. after solubilization. Alexa 488-labeled **K. pneumoniae OmpA** (p40) showed specific, dose-dependent binding to **dendritic** cells. Other possible carrier proteins, such as tetanus toxins and protein G derivs. did not bind **dendritic** cells. P40 is also internalized by **dendritic** cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1999:709825 HCAPLUS
DOCUMENT NUMBER:	132:34413
TITLE:	Carrier properties of a protein derived from **outer membrane protein A** of **Klebsiella pneumoniae**
AUTHOR(S):	Rauly, Isabelle; Goetsch, Liliane; Haeuw, Jean-Francois; Tardieux, Christine; Baussant, Thierry; Bonnefoy, Jean-Yves; Corvaia, Nathalie
CORPORATE SOURCE:	Centre d'Immunologie Pierre Fabre, Saint Julien en Genevois, Fr.
SOURCE:	Infection and Immunity (1999), 67(11), 5547-5551 CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The authors have recently cloned a new protein, recombinant P40 (rP40). When tested in vivo after conjugation to a **B-cell** epitope, rP40 induces an important antibody response without the need for adjuvant. To characterize its potency, this carrier protein was coupled to a peptide derived from respiratory syncytial virus attachment G protein (G1'). After immunization of mice with the rP40-G1' conjugate, strong antipeptide antibodies were detected, whereas peptide alone was not immunogenic. To emphasize the carrier properties of rP40, a polysaccharide derived from

Haemophilus influenzae type b (Hib) was coupled to it. IgG responses against the Hib polysaccharide were obsd. after coupling to rP40. Interestingly, an antipeptide antibody response was obsd. despite preexisting anti-rP40 antibodies generated by preimmunization with rP40. In addn., rP40 compares well with the ref. carrier protein, tetanus toxoid (TT), since antibody responses of equal intensity were obsd. when a peptide or a polysaccharide was coupled to TT and rP40. Moreover, rP40 had advantages compared to TT; e.g., it induced a mixed Th1/Th2 response, whereas TT induced only a Th2 profile. Together, the results indicate that rP40 is a novel carrier protein with potential for use as an alternative carrier for human vaccination.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, CANCERLIT' ENTERED AT 12:20:17 ON 07 AUG 2003)

L4 41 S L3

L5 20 DUP REM L4 (21 DUPLICATES REMOVED)

L5 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003039834 MEDLINE

DOCUMENT NUMBER: 22532491 PubMed ID: 12548563

TITLE: **Outer membrane protein A** renders **dendritic** cells and macrophages responsive to CCL21 and triggers **dendritic** cell migration to secondary lymphoid organs.

AUTHOR: Jeannin Pascale; Magistrelli Giovanni; Herbault Nathalie; Goetsch Liliane; Godefroy Sylvie; Charbonnier Peggy; Gonzalez Alexandra; Delneste Yves

CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, France.. pascale.jeannin@pierre-fabre.com

SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (2003 Feb) 33 (2) 326-33.
Journal code: 1273201. ISSN: 0014-2980.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200305

ENTRY DATE: Entered STN: 20030128
Last Updated on STN: 20030502
Entered Medline: 20030501

AB **Outer membrane protein A** (**OmpA**) is a class of bacterial cell wall protein that is immunogenic without adjuvant. As specific immune responses are initiated in the lymph nodes (LN, we analyzed the effect of the **OmpA** from **Klebsiella pneumoniae** (**KpOmpA**) onchemokine/ chemokine receptor expression by APC and on cell migration to the LN. Upon contact with **KpOmpA**, human immature DC and macrophages acquire CCR7 expression and responsiveness to CCL21. In parallel, CCR1 and CCR5 expression is down-regulated and CXCL8, CCL2, CCL3 and CCL5 production is up-regulated. Mice injected subcutaneously with **KpOmpA** present a transient inflammatory reaction at the site of injection accompanied by an enlargement of the draining LN with a higher

proportion of DC and macrophages. Lastly, when exposed to **KpOmpA** prior injection, DC but not macrophages migrate to the draining LN. In conclusion, **KpOmpA** confers a migratory phenotype to DC and triggers their migration to the regional LN. This property contributes to explain how innate cells initiate adaptive immune response upon recognition of conserved bacterial components and also why **OmpA** is immunogenic in the absence of adjuvant.

L5 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003229889 IN-PROCESS
DOCUMENT NUMBER: 22636479 PubMed ID: 12751905
TITLE: **Outer membrane protein A** (**OmpA**) activates human epidermal Langerhans cells.
AUTHOR: Godefroy Sylvie; Corvaia Nathalie; Schmitt Daniel; Aubry Jean-Pierre; Bonnefoy Jean-Yves; Jeannin Pascale; Staquet Marie-Jeanne
CORPORATE SOURCE: INSERM U346, affilie CNRS, Hopital E. Herriot, Lyon, France.
SOURCE: EUROPEAN JOURNAL OF CELL BIOLOGY, (2003 Apr) 82 (4) 193-200.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030520
Last Updated on STN: 20030520

AB Outer membrane protein (**Omp**)**A** is highly represented and conserved in the **Enterobacteriaceae** family. Using a recombinant **OmpA** from **Klebsiella pneumoniae** (**kpOmpA**), we have analysed the interaction between this bacterial cell wall protein and human Langerhans cells (LC), the **antigen**-presenting **cells** of the epidermis and mucosa. We showed that biotinylated **kpOmpA** binds to human LC freshly isolated from epidermis. **kpOmpA** up-regulated MHC class II, CD86 and CCR7 expression, enhanced migration in response to macrophage inflammatory protein-3beta (MIP-3beta) through a reconstituted basement membrane mimicking the prerequisite passage through the dermal-epidermal basement membrane on the way to lymph nodes. The allostimulatory function of **kpOmpA**-treated LC was more potent than that of untreated cells. Even though the proportion of LC which binds **kpOmpA** was shown to vary between individuals, our data indicate that **kpOmpA** binds to and activates LC, and suggest that recognition of **OmpA** by LC may be an initiating event in the antibacterial host response.

L5 ANSWER 3 OF 20 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002272905 MEDLINE
DOCUMENT NUMBER: 22008439 PubMed ID: 12009270
TITLE: Streptococcus pneumoniae polysaccharides conjugated to the **outer membrane protein A** from **Klebsiella pneumoniae** elicit protective antibodies.
AUTHOR: Libon Christine; Haeuw Jean Francois; Crouzet Francoise; Mugnier Chantal; Bonnefoy Jean Yves; Beck

Alain; Corvaia Nathalie
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, 5 Avenue Napoleon III, St. Julien en Genevois, France..
christine.libon@pierre-fabre.com
SOURCE: VACCINE, (2002 May 22) 20 (17-18) 2174-80.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020516
Last Updated on STN: 20030102
Entered Medline: 20021231

AB Polysaccharides (PSs) derived from Streptococcus pneumoniae include more than 90 serotypes and differ greatly in their immunogenicity. In addition, immunization with PSs does not induce high affinity antibody production and no memory **B-cells** are generated. Coupling PSs to carrier proteins has been reported to induce **B-cell** maturation and to install a **B-cell** memory. As an alternative carrier protein, the **outer membrane protein A** (**OmpA**) derived from **Klebsiella pneumoniae** has been coupled to various PSs. We evaluated the immunogenicity of two PS conjugates, using PS derived from S. pneumoniae types 14 and 19. In this report, we show that anti-PS IgG responses are generated after the conjugation of PSs to P40. In addition, the humoral response generated is able to protect mice from a bacterial challenge. Our results indicate that P40 could be included in the development of new PS conjugate vaccines.

L5 ANSWER 4 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:46057 BIOSIS
DOCUMENT NUMBER: PREV200300046057
TITLE: Strategy of Escherichia coli for crossing the blood-brain barrier.
AUTHOR(S): Kim, Kwang Sik (1)
CORPORATE SOURCE: (1) Division of Pediatric Infectious Diseases, Johns Hopkins University School of Medicine, 600 N. Wolfe St., Park 256, Baltimore, MD, 21287, USA: kwangkim@jhmi.edu USA
SOURCE: Journal of Infectious Diseases, (1 December 2002) Vol. 186, No. Supplement 2, pp. S220-S224. print.
ISSN: 0022-1899.
DOCUMENT TYPE: Article
LANGUAGE: English

AB A major contributing factor to high mortality and morbidity associated with bacterial meningitis is the incomplete understanding of the pathogenesis of this disease: It is unclear how circulating bacteria cross the blood-brain barrier (BBB). Recent studies with Escherichia coli K1 show that successful traversal of the BBB requires a high degree of bacteremia, invasion of brain microvascular endothelial cells (BMEC), host cell actin cytoskeleton rearrangements and related signaling pathways, and traversal of the BBB as live bacteria. Several microbial determinants such as the K1 capsule, **OmpA**, Ibe proteins, AsIA, TraJ, and CNF1 contribute to BMEC invasion. Of interest, E. coli K1 trafficking

mechanisms differ from those of other meningitis-causing bacteria such as Listeria **monocytogenes** and group B streptococcus. Complete understanding of bacteria-BMEC interactions contributing to translocation of the BBB should assist in developing novel strategies to prevent bacterial meningitis.

L5 ANSWER 5 OF 20 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002716404 MEDLINE
DOCUMENT NUMBER: 22366614 PubMed ID: 12477424
TITLE: **Outer membrane protein A (OmpA)**: a new pathogen-associated molecular pattern that interacts with **antigen** presenting **cells**-impact on vaccine strategies.
AUTHOR: Jeannin Pascale; Magistrelli Giovanni; Goetsch Liliane; Haeuw Jean-Francois; Thieblemont Nathalie; Bonnefoy Jean-Yves; Delneste Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, 5, Avenue Napoleon III, F-74164 Saint-Julien en Genevois, France.. pascale.jeannin@pierre-fabre.com
SOURCE: VACCINE, (2002 Dec 19) 20 Suppl 4 A23-7. Ref: 31
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030715
Entered Medline: 20030714

AB **Outer membrane protein A (OmpA)** is a class of proteins highly conserved among the **Enterobacteriaceae** family and throughout evolution. We have observed that **antigen** presenting **cells** (APCs) recognize and are activated by the recombinant **OmpA** from **Klebsiella pneumoniae (KpOmpA)**. **KpOmpA** triggers cytokine production by macrophages and **dendritic** cells (**DC**), induces **DC** maturation and signals via Toll-like receptor 2. **KpOmpA** also interacts with endocytic receptor(s) expressed on DC and macrophages. Tumor antigens coupled to **KpOmpA** are taken up by APCs and gain access to the MHC class I pathway, triggering the initiation of protective anti-tumor cytotoxic responses in the absence of CD4 T cell help and adjuvant. Thus, **OmpA** appears as a new type of pathogen-associated molecular pattern (PAMP) usable as a vector in anti-infectious and therapeutic anti-tumor vaccines to elicit CTLs.

L5 ANSWER 6 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2001459913 MEDLINE
DOCUMENT NUMBER: 21185102 PubMed ID: 11286869
TITLE: DC targeting by a bacterial **OmpA**.
AUTHOR: Blacklaws B
SOURCE: TRENDS IN MICROBIOLOGY, (2001 Apr) 9 (4) 159.
Journal code: 9310916. ISSN: 0966-842X.
PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

L5 ANSWER 7 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-055641 [07] WPIDS
DOC. NO. CPI: C2002-015986
TITLE: Use of an **enterobacterium OmpA** protein for prophylactic and therapeutic treatment of viral, bacterial, fungal and parasitic infections.
DERWENT CLASS: B04
INVENTOR(S): BAUSSANT, T; DELNESTE, Y; JEANNIN, P
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001087326	A1	20011122	(200207)*	FR	33
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU BR CA CN JP MX US ZA					
FR 2809014	A1	20011123	(200207)		
AU 2001062423	A	20011126	(200222)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001087326	A1	WO 2001-FR1490	20010516
FR 2809014	A1	FR 2000-6199	20000516
AU 2001062423	A	AU 2001-62423	20010516

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001062423	A	Based on	WO 200187326

PRIORITY APPLN. INFO: FR 2000-6199 20000516
AN 2002-055641 [07] WPIDS
AB WO 200187326 A UPAB: 20020130
NOVELTY - Use of an **enterobacterium OmpA** protein, or one of its fragments or protein derivatives to prepare an antimicrobial pharmaceutical composition in which the concentration of the **OmpA** protein is between 0.08 and 1 mu M.

ACTIVITY - Antibacterial; antifungal; antiviral; antiparasitic.
MECHANISM OF ACTION - Microphage activation inducer.
USE - Prophylactic and therapeutic treatment of viral, bacterial, fungal and parasitic infections.

Mononucleated cells from human peripheral blood were purified using a Ficoll slope and the resultant **monocytes** purified by positive selection using a magnetic cell separator. These

monocytes were cultured for 5 - 7 days with 10 ng/ml of granulocyte macrophage colony stimulating factor to 5x106 cells per 5 ml well in a 6-well culture plate containing 10% calf fetal serum, 50 U/ml penicillin, 2 mM glutamine, 50 mg/ml streptomycin, 10 mM HEPES buffer and 0.1 mM non-essential amino acids. This gave human microphages. These were incubated with the **OmpA** protein derived from **Klebsiella pneumoniae** having sequence SEQ ID NO.1 given in the patent. Cytofluorometric analysis showed strong binding that was concentration dependent.
Dwg.0/3

L5 ANSWER 8 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-066490 [09] WPIDS
DOC. NO. NON-CPI: N2002-049378
DOC. NO. CPI: C2002-019799
TITLE: Composition, useful for treatment and prevention of cancer, also for detecting tumor antigens, comprises an outer membrane protein and tumor lysate.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BONNEFOY, J Y; INVERNIZZI, I; RENNO, T; BONNEFOY, J
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001082959	A1	20011108	(200209)*	FR	31
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU BR CA CN JP MX US ZA					
FR 2808445	A1	20011109	(200209)		
AU 2001058481	A	20011112	(200222)		
EP 1278539	A1	20030129	(200310)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001082959	A1	WO 2001-FR1348	20010503
FR 2808445	A1	FR 2000-5702	20000504
AU 2001058481	A	AU 2001-58481	20010503
EP 1278539	A1	EP 2001-931780	20010503
		WO 2001-FR1348	20010503

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001058481	A	Based on	WO 200182959
EP 1278539	A1	Based on	WO 200182959

PRIORITY APPLN. INFO: FR 2000-5702 20000504
AN 2002-066490 [09] WPIDS
AB WO 200182959 A UPAB: 20020208
NOVELTY - Pharmaceutical composition (A), comprising at least one outer membrane protein (Omp; I) or its fragment, associated with a lysate (B) of autologous and/or heterologous tumor cells, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) device containing at least one (I) and a system for preparing (A); and

(2) detecting tumor antigens.

ACTIVITY - Cytostatic. No biological data was provided.

MECHANISM OF ACTION - Induction, or enhancement, of an immune response, particularly cytotoxic T cells, against tumors, resulting in growth inhibition.

USE - (A) are used (i) for treatment or prevention of cancers, particularly where associated with tumor antigens and (ii) for detecting tumor antigens. B16 melanoma cells were implanted subcutaneously in mice which were injected, on the same day, with (i) 350 mu g P40 (Omp of **Klebsiella pneumoniae**) and the lysate of 106 B16 cells or (ii) the lysate only. The treatment was repeated on day 10, and on day 18 tumor volume was measured. This was 2000 to over 4000 mm3 for (ii) but less than 1000 mm3 for (i).

ADVANTAGE - (A) can be used to treat cancer in its early stages and has few if any side effects. (I) bind tumor antigens specifically and at a higher level than conventional carriers.

Dwg.0/3

L5 ANSWER 9 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2001-427232 [46] WPIDS

DOC. NO. CPI: C2001-129432

TITLE: Preparing purified polypeptide soluble in absence of detergent, useful for modulating the immune system, e.g. in vaccines, by removal of detergent, denaturing and molecular sieving.

DERWENT CLASS: B04 D16

INVENTOR(S): BAUSSANT, T; BONNEFOY, J; DELNESTE, Y; JEANNIN, P; LAWNY, F; BONNEFOY, J Y; JHEANNIN, P

PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE; (BAUS-I) BAUSSANT T; (BONN-I) BONNEFOY J; (DELN-I) DELNESTE Y; (JEAN-I) JEANNIN P; (LAWN-I) LAWNY F

COUNTRY COUNT: 34

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2803302	A1	20010706	(200146)*		34
WO 2001049705	A2	20010712	(200146)	FR	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU BR CA CN JP MX US ZA					
AU 2001031837	A	20010716	(200169)		
EP 1244690	A2	20021002	(200265)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001007421	A	20021022	(200278)		
US 2003044915	A1	20030306	(200320)		
ZA 2002004930	A	20030430	(200334)		77
CN 1396927	A	20030212	(200335)		
JP 2003519238	W	20030617	(200349)		45

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

FR 2803302	A1	FR 2000-70	20000104
WO 2001049705	A2	WO 2001-FR23	20010104
AU 2001031837	A	AU 2001-31837	20010104
EP 1244690	A2	EP 2001-903868	20010104
		WO 2001-FR23	20010104
BR 2001007421	A	BR 2001-7421	20010104
		WO 2001-FR23	20010104
US 2003044915	A1	WO 2001-FR23	20010104
		US 2002-169953	20020703
ZA 2002004930	A	ZA 2002-4930	20020619
CN 1396927	A	CN 2001-804096	20010104
JP 2003519238	W	JP 2001-550245	20010104
		WO 2001-FR23	20010104

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001031837	A	Based on	WO 200149705
EP 1244690	A2	Based on	WO 200149705
BR 2001007421	A	Based on	WO 200149705
JP 2003519238	W	Based on	WO 200149705

PRIORITY APPLN. INFO: FR 2000-70 20000104

AN 2001-427232 [46] WPIDS

AB FR 2803302 A UPAB: 20010815

NOVELTY - Preparation (M1) of a purified solution of a polypeptide (I) that is soluble in aqueous solvent in absence of detergent (II), comprising:

(i) removing (II);

(ii) solubilizing (I) in solution of denaturing agent; and

(iii) eluting, in aqueous solution, soluble (I) by molecular sieving column chromatography, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) water-soluble (I) produced by M1;

(b) modulating the immune system in mammals towards an antigen by inducing maturation of isolated **dendritic** cells (**DC**) in the presence of (I); and

(c) modulating the immune system in a mammal by injecting (I), alone or as adjuvant.

ACTIVITY - Immunomodulatory; immunostimulatory; antiviral; anti-human immunodeficiency virus; antibacterial; anticancer; antimycotic; antifungal; antiparasitic; cardiant; anti-inflammatory.

MECHANISM OF ACTION - Vaccine. The preferred (I), **outer membrane protein A** (P40) of **Klebsiella pneumoniae**, binds selectively to **antigen**-presenting **cell**, so provides targeting, proliferation and/or expression of molecules by these cells. Recombinant soluble P40 was conjugated to ovalbumin and the composition used to inject mice. Spleen cells were incubated with irradiated E.G7 cells and then tested (as effector) against chromium-labeled target cells (EL4, pulsed with E.G7 and the peptide SIINFEKL). Specific lysis at effector:target ratio 100:1 was 40%, comparable with that for a conjugate of non-solubilized P40.

USE - (I) are used, alone or as an adjuvant, to produce therapeutic compositions that are soluble in absence of (II),

especially when formulated with an antigen or hapten (A) for modulating the host's immune system. Especially they are used to prepare vaccines, especially antiviral, antibacterial or anticancer (e.g. against human immune deficiency virus, respiratory syncytial virus, measles, mumps, tuberculosis etc.), but also (not claimed) against fungi, parasites, autoimmune diseases, graft rejection, cardiovascular disease, inflammation and immune deficiency.

ADVANTAGE - (I) can be administered without co-injection of potentially harmful detergents, and may have an altered tertiary structure that affects biological activity, particularly causing an alteration that renders (I) hydrophilic. They are particularly useful for use with weakly immunogenic antigens or haptens.

Dwg.0/6

L5 ANSWER 10 OF 20 TOXCENTER COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	2001:136651 TOXCENTER
COPYRIGHT:	Copyright 2003 ACS
DOCUMENT NUMBER:	CA13508106360P
TITLE:	Solubilization of proteins for antigen use in an aqueous solvent without using detergents
AUTHOR(S):	Baussant, Thierry; Jeannin, Pascale; Delneste, Yves; Lawny, Francois; Bonnefoy, Jean-Yves
CORPORATE SOURCE:	ASSIGNEE: Pierre Fabre Medicament
PATENT INFORMATION:	WO 2001049705 A2 12 Jul 2001
SOURCE:	(2001) PCT Int. Appl., 37 pp. CODEN: PIXXD2.
COUNTRY:	FRANCE
DOCUMENT TYPE:	Patent
FILE SEGMENT:	CAPLUS
OTHER SOURCE:	CAPLUS 2001:507718
LANGUAGE:	French
ENTRY DATE:	Entered STN: 20011116 Last Updated on STN: 20020319

AB The invention concerns a novel method for prepg. a polypeptide sol. in an aq. solvent in the absence of detergent, and polypeptides obtainable by said method. The invention also concerns the use of said polypeptides, in particular for prepg. medicines or vaccines, against bacterial and viral infections or cancers. Specifically, the method is used for hydrophobic membrane proteins such as porins to allow them to be used in vaccines without the use of detergents. The **ompA** porin (rP40) of **Klebsiella pneumoniae** was manufd. by expression of the cloned gene in EScherichia coli where it accumulated as inclusion bodies. The inclusion bodies were recovered from lysates by centrifugation and solubilized in urea 7M, dithiothreitol 10 mM, Tris HCl (25 mM, pH 8.5) at 37.degree. for 2h. The solubilized material was dild. with 13 vols. of NaCl (8.76 g/L), Zwittergent 3-14 (0.1 vol%), Tris HCl (25 mM, pH 8.5) and allowed to renature overnight at room temp. and desalted by dialysis against Tris HCl (25 mM, pH 8.5), Zwittergent 3-14 (0.1 vol%) at 4.degree.. The dialyzed material was purified by ion-exchange chromatog. against strong anion and cation exchangers to yield a protein solubilized with Zwittergent 3-14. The purified protein was pptd. with 5 vols. of ethanol, resolubilized in urea 7M as before to yield a stable hydrophilic form that was predominantly .alpha.-helical as opposed to the hydrophilic .beta.-sheet protein. The protein was able to induce CD38 synthesis and interleukin 12 secretion in human **dendritic** cells. The effects were polymyxin B sensitive and therefore not due to contaminating

endotoxins.

L5 ANSWER 11 OF 20 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001503887 MEDLINE
DOCUMENT NUMBER: 21437651 PubMed ID: 11553588
TITLE: Targeting of nasal mucosa-associated **antigen**-presenting **cells** in vivo with an **outer membrane protein A** derived from **Klebsiella pneumoniae**.
AUTHOR: Goetsch L; Gonzalez A; Plotnicky-Gilquin H; Haeuw J F; Aubry J P; Beck A; Bonnefoy J Y; Corvaia N
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, 74164 Saint-Julien en Genevois, France.. liliane.goetsch@pierre-fabre.com
SOURCE: INFECTION AND IMMUNITY, (2001 Oct) 69 (10) 6434-44. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010913
Last Updated on STN: 20011029
Entered Medline: 20011025

AB Administration of vaccines by the nasal route has recently proven to be one of the most efficient ways for inducing both mucosal and systemic antibody responses in experimental animals. Our results demonstrate that P40, a well-defined **outer membrane protein A** from **Klebsiella pneumoniae**, is indeed a carrier molecule suitable for nasal immunization. Using fragments from the respiratory syncytial virus subgroup A (RSV-A) G protein as antigen models, it has been shown that P40 is able to induce both systemic and mucosal immunity when fused or coupled to a protein or a peptide and administered intranasally (i.n.) to naive or **K. pneumoniae**-primed mice. Confocal analyses of nasal mucosa-associated lymphoid tissue after i.n. instillation of P40 showed that this molecule is able to cross the nasal epithelium and target CD11c-positive cells likely to be murine **dendritic** cells or macrophages. More importantly, this targeting of **antigen**-presenting **cells** following i.n. immunization with a subunit of the RSV-A molecule in the absence of any mucosal adjuvant results in both upper and lower respiratory tract protection against RSV-A infection.

L5 ANSWER 12 OF 20 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002135865 MEDLINE
DOCUMENT NUMBER: 21840737 PubMed ID: 11851331
TITLE: Stability and CTL-activity of P40/ELA melanoma vaccine candidate.
AUTHOR: Beck A; Goetsch L; Champion T; Bussat M C; Aubry J P; Klinguer-Hamour C; Haeuw J F; Bonnefoy J Y; Corvaia N
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre (CIPF), bioMerieux-Pierre Fabre, 5 Avenue Napoleon III, F-74164 Saint-Julien-en-Genevois, France.. alain.beck@pierre-fabre.com
SOURCE: BIOLOGICALS, (2001 Sep-Dec) 29 (3-4) 293-8.

Journal code: 9004494. ISSN: 1045-1056.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020302
Last Updated on STN: 20020503
Entered Medline: 20020502

AB The decapeptide ELA (ELAGIGILTV), a Melan-A/MART-1 antigen immunodominant peptide analogue, is an interesting melanoma vaccine candidate alone or in combination with other tumour antigens. P40, the recombinant **outer membrane protein A** of **Klebsiella pneumoniae** (**kpOmpA**), was recently shown to target **dendritic** cells and to induce peptide-specific CTLs. Here we investigated the adjuvant role of P40 mixed or chemically conjugated to ELA. This compound is an N-terminal glutamic acid-containing peptide. However, it has been reported that the amino group and the gamma-carboxylic group of glutamic acids easily condense to form pyroglutamic derivatives. Usually, to overcome this stability problem, peptides of pharmaceutical interest were developed with a pyroglutamic acid instead of N-terminal glutamic acid, without loss of pharmacological properties. Unfortunately, the pyroglutamic acid derivative (PyrELA) as well as the N-terminal acetyl capped derivative (AcELA) failed to elicit CTL activity when mixed with P40 adjuvant protein. Despite the apparent minor modifications introduced by PyrELA and AcELA, these two derivatives have probably lower affinity than ELA for the class I Major Histocompatibility Complex. Furthermore, this stability problem is worse in the case of clinical grade ELA, produced as an acetate salt, like most of the pharmaceutical grade peptides. We report here that the hydrochloride shows a higher stability than the acetate and may be suitable for use in man.

L5 ANSWER 13 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001123310 EMBASE
TITLE: DC targeting by a bacterial **OmpA**.
AUTHOR: Blacklaws B.
CORPORATE SOURCE: . bab2@cam.ac.uk
SOURCE: Trends in Microbiology, (1 Apr 2001) 9/4 (159).
Refs: 1
ISSN: 0966-842X CODEN: TRMIEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

L5 ANSWER 14 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
DUPLICATE 7
ACCESSION NUMBER: 2000-387342 [33] WPIDS
DOC. NO. CPI: C2000-117516
TITLE: Use of **enterobacterial outer membrane protein A** for delivering active substances, particularly immunogens for treating or preventing e.g. cancer, to **antigen** presenting **cells**.

DERWENT CLASS: B04 D16
INVENTOR(S): AUBRY, J P; BAUSSANT, T; BONNEFOY, J Y; JEANNIN, P; LECOANET, S; AUBRY, J; BONNEFOY, J
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000027432	A1	20000518	(200033)*	FR	34
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CN JP MX US ZA					
FR 2785542	A1	20000512	(200033)		
AU 2000011641	A	20000529	(200041)		
BR 9915071	A	20010717	(200146)		
EP 1124577	A1	20010822	(200149)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1326360	A	20011212	(200225)		
MX 2001004571	A1	20010701	(200236)		
ZA 2001003478	A	20020424	(200237)		54
JP 2002529428	W	20020910	(200274)		37

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000027432	A1	WO 1999-FR2734	19991108
FR 2785542	A1	FR 1998-14007	19981106
AU 2000011641	A	AU 2000-11641	19991108
BR 9915071	A	BR 1999-15071	19991108
		WO 1999-FR2734	19991108
EP 1124577	A1	EP 1999-971719	19991108
		WO 1999-FR2734	19991108
CN 1326360	A	CN 1999-813453	19991108
MX 2001004571	A1	MX 2001-4571	20010504
ZA 2001003478	A	ZA 2001-3478	20010430
JP 2002529428	W	WO 1999-FR2734	19991108
		JP 2000-580661	19991108

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000011641	A	Based on	WO 200027432
BR 9915071	A	Based on	WO 200027432
EP 1124577	A1	Based on	WO 200027432
JP 2002529428	W	Based on	WO 200027432

PRIORITY APPLN. INFO: FR 1998-14007 19981106
AN 2000-387342 [33] WPIDS
AB WO 200027432 A UPAB: 20000712
NOVELTY - Use of a pharmaceutical composition comprising an **outer membrane protein A** (**OmpA**), or its fragments, for specific targeting of an active substance (I) to **antigen**-presenting **cells** (APC).
ACTIVITY - Cytostatic; anti-allergic; cardiovascular; anti-inflammatory; anti-microbial; immunostimulatory.
MECHANISM OF ACTION - Induction of a specific immune response.

USE - **OmpA** is used to deliver an antigen or hapten to modify (specifically to improve) an immune response, especially for treatment or prevention of cancers (particularly those that express a tumor-associated antigen), autoimmune disease, allergy, graft rejection, cardiovascular or central nervous system diseases, inflammation, infection or immune deficiency.

ADVANTAGE - **OmpA** binds specifically to APCs and is internalized by them (contrast other protein carriers such as tetanus toxoid).

Dwg.0/5

L5 ANSWER 15 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:469761 BIOSIS
DOCUMENT NUMBER: PREV200000469761
TITLE: Bacterial penetration across the blood-brain barrier during the development of neonatal meningitis.
AUTHOR(S): Huang, Sheng-He (1); Stins, Monique F.; Kim, Kwang Sik
CORPORATE SOURCE: (1) Division of Infectious Diseases, Childrens Hospital Los Angeles, University of Southern California, Los Angeles, CA, 90027 USA
SOURCE: Microbes and Infection, (August, 2000) Vol. 2, No. 10, pp. 1237-1244. print.
ISSN: 1286-4579.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Bacterial pathogens may breach the blood-brain barrier (BBB) and invade the central nervous system through paracellular and/or transcellular mechanisms. Transcellular penetration, e.g., transcytosis across the BBB has been demonstrated for Escherichia coli, K1, group B streptococcus, Listeria **monocytogenes**, Citrobacter freundii and Streptococcus pneumonia strains. Genes contributing to invasion of brain microvascular endothelial cells include E. coli K1 genes **ompA**, ibeA, ibeB, and jijP. Understanding the mechanisms of bacterial penetration across the BBB may help develop novel approaches to preventing bacterial meningitis.

L5 ANSWER 16 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:509530 BIOSIS
DOCUMENT NUMBER: PREV200000509530
TITLE: Highly efficient selection of phage antibodies mediated by display of antigen as Lpp-**OmpA**' fusions on life bacteria.
AUTHOR(S): Benhar, Itai (1); Azriel, Ronit; Nahary, Limor; Shaky, Shelly; Berdichevsky, Yevgeny; Tamarkin, Aviva; Wels, Winfried
CORPORATE SOURCE: (1) Department of Molecular Microbiology and Biotechnology, The George S. Wise Faculty of Life Sciences, Tel-Aviv University, Green Building, Room 202, Ramat Aviv, 69978 Israel
SOURCE: Journal of Molecular Biology, (25 August, 2000) Vol. 301, No. 4, pp. 893-904. print.
ISSN: 0022-2836.
DOCUMENT TYPE: Article

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Delayed infectivity panning (DIP) is a novel approach for the in vivo isolation of interacting protein pairs. DIP combines phage display and cell surface display of polypeptides as follows: an antigen is displayed in many copies on the surface of F+ Escherichia coli cells by fusing it to a Lpp-**OmpA'** hybrid. To prevent premature, non-specific infection by phage, the cells are rendered functionally F- by growth at 16degreeC. The **antigen** -displaying **cells** are used to capture antibody-displaying phage by virtue of the antibody-antigen interaction. Following removal of unbound phage, infection of the cells by bound phage is initiated by raising the temperature to 37degreeC that facilitates F pilus expression. The phage then dissociate from the antigen and infect the bacteria through the F pilus. Using specific scFv antibodies and the human ErbB2 proto-oncogene and IL2-Ralpha chain as model antibody-antigen pairs, we demonstrate enrichment of those phage that display a specific antibody over phage that display an irrelevant antibody of over 1,000,000 in a single DIP cycle. We further show the successful isolation of anti-toxin, anti-receptor, anti-enzyme and anti-peptide antibodies from several immune phage libraries, a shuffled library and a large synthetic human library. The effectiveness of DIP makes it suitable for the isolation of rare clones present in large libraries. Since DIP can be applied for most of the phage libraries already existing, it could be a powerful tool for the rapid isolation and characterization of binders in numerous protein-protein interactions.

L5 ANSWER 17 OF 20 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001175127 MEDLINE
DOCUMENT NUMBER: 21170020 PubMed ID: 11101872
TITLE: **OmpA** targets **dendritic** cells, induces their maturation and delivers antigen into the MHC class I presentation pathway.
AUTHOR: Jeannin P; Renno T; Goetsch L; Miconnet I; Aubry J P; Delneste Y; Herbault N; Baussant T; Magistrelli G; Soulas C; Romero P; Cerottini J C; Bonnefoy J Y
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, 5, Avenue Napoleon III, F-74164 Saint-Julien en Genevois, France.. pascale.jeannin@pierre-fabre.com
SOURCE: Nat Immunol, (2000 Dec) 1 (6) 502-9. Journal code: 100941354. ISSN: 1529-2908.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010417
Last Updated on STN: 20010417
Entered Medline: 20010412
AB We analyzed the interaction between a bacterial cell wall protein and **dendritic** cells (**DCs**). **Outer membrane protein A** from **Klebsiella pneumoniae** (**kpOmpA**) specifically bound to professional **antigen** presenting **cells** and was endocytosed by immature DCs via a receptor-dependent mechanism. **kpOmpA** signaled through Toll-like receptor 2, induced DCs to produce interleukin 12 and

induced maturation of DCs. Whole antigen that was coupled to **kpOmpA** and injected into mice was taken up by DCs and delivered to the conventional cytosolic MHC class I presentation pathway. **kpOmpA** also primed antigen-specific CD8+ CTLs in the absence of CD4+ T cell help or adjuvant and elicited therapeutic immunity to antigen-expressing tumors. Thus, **OmpA** belongs to a class of proteins that are able to elicit CTL responses to exogenous antigen.

L5 ANSWER 18 OF 20 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2000002524 MEDLINE
DOCUMENT NUMBER: 20002524 PubMed ID: 10531198
TITLE: Carrier properties of a protein derived from **outer membrane protein A** of **Klebsiella pneumoniae**
.
AUTHOR: Rauly I; Goetsch L; Haeuw J F; Tardieux C; Baussant T; Bonnefoy J Y; Corvaia N
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint Julien en Genevois, France.
SOURCE: INFECTION AND IMMUNITY, (1999 Nov) 67 (11) 5547-51. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991116

AB We have recently cloned a new protein, recombinant P40 (rP40). When tested in vivo after conjugation to a **B-cell** epitope, rP40 induces an important antibody response without the need for adjuvant. To characterize its potency, this carrier protein was coupled to a peptide derived from respiratory syncytial virus attachment G protein (G1'). After immunization of mice with the rP40-G1' conjugate, strong antipeptide antibodies were detected, whereas peptide alone was not immunogenic. To emphasize the carrier properties of rP40, a polysaccharide derived from Haemophilus influenzae type b (Hib) was coupled to it. Immunoglobulin G responses against the Hib polysaccharide were observed after coupling to rP40. Interestingly, an antipeptide antibody response was observed despite preexisting anti-rP40 antibodies generated by preimmunization with rP40. In addition, rP40 compares well with the reference carrier protein, tetanus toxoid (TT), since antibody responses of equal intensity were observed when a peptide or a polysaccharide was coupled to TT and rP40. Moreover, rP40 had advantages compared to TT; e.g., it induced a mixed Th1/Th2 response, whereas TT induced only a Th2 profile. Together, the results indicate that rP40 is a novel carrier protein with potential for use as an alternative carrier for human vaccination.

L5 ANSWER 19 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:586000 BIOSIS
DOCUMENT NUMBER: PREV199497005370
TITLE: The 39-kilodalton outer membrane protein of Proteus mirabilis is an **OmpA** protein and mitogen

for murine **B lymphocytes**.

AUTHOR(S): Korn, Alexander; Kroll, Hein-Peter; Berger, Hans-Peter; Kahler, Andrea; Hessler, Regina; Brauburger, Jens; Mueller, Klaus-Peter; Nixdorff, Kathryn (1)

CORPORATE SOURCE: (1) Dep. Microbiol., University Darmstadt, Schnittspahnstr. 10, D-64287 Darmstadt Germany

SOURCE: Infection and Immunity, (1993) Vol. 61, No. 11, pp. 4915-4918.
ISSN: 0019-9567.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Partial amino acid sequence analysis of a major outer membrane protein of Proteus mirabilis (39-kDa protein) indicates that it is an **OmpA** protein. The mitogenic activities of the 39-kDa protein for murine lymphocytes were also investigated with T lymphocytes isolated by passing spleen cells over columns of nylon wool fiber and **B lymphocytes** obtained by treating spleen cells with monoclonal antibodies to Thy1 plus complement. The 39-kDa protein showed little activity in stimulating T cells to proliferate but was strongly mitogenic for **B cells**.

L5 ANSWER 20 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1993:320305 BIOSIS

DOCUMENT NUMBER: PREV199396028655

TITLE: Characterization of a heat-modifiable outer membrane protein of Haemophilus somnus.

AUTHOR(S): Tagawa, Yuichi (1); Haritani, Makoto; Ishikawa, Hitoshi; Yuasa, Noboru

CORPORATE SOURCE: (1) Natl. Inst. Animal Health, 3-1-1- Kannondai, Tsukuba, Ibaraki 305 Japan

SOURCE: Infection and Immunity, (1993) Vol. 61, No. 5, pp. 1750-1755.
ISSN: 0019-9567.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In immunoblot analysis, a murine monoclonal antibody (MAb), 27-1, which was produced to an outer membrane protein (OMP) of Haemophilus somnus, showed that a major OMP is heat modifiable, having a molecular mass of 28 kDa when the N-lauroylsarcosine-insoluble OMP preparation was solubilized at 60 degree C and a mass of 37 kDa when the OMP preparation was solubilized at 100 degree C. The heat-modifiable OMP reacted intensely with convalescent sera obtained from calves with experimental H. somnus pneumonia in immunoblot analysis. Immunoelectron microscopic and antibody absorption studies revealed that the MAb 27-1 epitope was not surface exposed on the intact bacterium. However, a decrease in antibody reactivity to the heat-modifiable OMP in immunoblot analysis after absorption of convalescent serum with intact bacterial cells of H. somnus suggests that a surface-exposed portion of the heat-modifiable OMP is expressed on the intact bacterium. MAb 27-1 reacted with 45 of 45 strains of H. somnus tested in immunoblot analysis. The apparent molecular mass of the antigen varied among strains, and five reactivity patterns demonstrated by MAb 27-1 were observed. MAb 27-1 also reacted with six species in the family Pasteurellaceae, Escherichia coli, and Salmonella dublin, but not

with the other eight species of gram-negative bacteria. The heat-modifiable OMP of H. somnus showed immunological cross-reactivity with the **OmpA** protein of E. coli K-12 and significant N-terminal amino acid sequence homology with the **OmpA** proteins of gram-negative bacteria. We conclude that a major, 37-kDa heat-modifiable OMP of H. somnus, which elicits an antibody response in H. somnus-infected animals, is a common antigen among H. somnus strains tested and is structurally related to the **OmpA** protein of E. coli.

(FILE 'MEDLINE' ENTERED AT 12:23:58 ON 07 AUG 2003)

L6	5460	SEA FILE=MEDLINE ABB=ON	PLU=ON	"KLEBSIELLA PNEUMONIAE"/CT
L7	9701	SEA FILE=MEDLINE ABB=ON	PLU=ON	"BACTERIAL OUTER MEMBRANE PROTEINS"/CT
L8	82	SEA FILE=MEDLINE ABB=ON	PLU=ON	L6 AND L7
L9	8311	SEA FILE=MEDLINE ABB=ON	PLU=ON	"DENDRITIC CELLS"/CT
L10	30545	SEA FILE=MEDLINE ABB=ON	PLU=ON	MONOCYTES/CT
L11	49724	SEA FILE=MEDLINE ABB=ON	PLU=ON	B-LYMPHOCYTES/CT
L12	4	SEA FILE=MEDLINE ABB=ON	PLU=ON	L8 AND (L9 OR L10 OR L11)

L12 ANSWER 1 OF 4 MEDLINE on STN
AN 2001459913 MEDLINE
TI DC targeting by a bacterial OmpA.
AU Blacklaws B
SO TRENDS IN MICROBIOLOGY, (2001 Apr) 9 (4) 159.
Journal code: 9310916. ISSN: 0966-842X.

L12 ANSWER 2 OF 4 MEDLINE on STN
AN 2001175127 MEDLINE
TI OmpA targets dendritic cells, induces their maturation and delivers antigen into the MHC class I presentation pathway.
AU Jeannin P; Renno T; Goetsch L; Miconnet I; Aubry J P; Delneste Y; Herbault N; Baussant T; Magistrelli G; Soulas C; Romero P; Cerottini J C; Bonnefoy J Y
SO Nat Immunol, (2000 Dec) 1 (6) 502-9.
Journal code: 100941354. ISSN: 1529-2908.
AB We analyzed the interaction between a bacterial cell wall protein and dendritic cells (DCs). Outer membrane protein A from Klebsiella pneumoniae (kpOmpA) specifically bound to professional antigen presenting cells and was endocytosed by immature DCs via a receptor-dependent mechanism. kpOmpA signaled through Toll-like receptor 2, induced DCs to produce interleukin 12 and induced maturation of DCs. Whole antigen that was coupled to kpOmpA and injected into mice was taken up by DCs and delivered to the conventional cytosolic MHC class I presentation pathway. kpOmpA also primed antigen-specific CD8+ CTLs in the absence of CD4+ T cell help or adjuvant and elicited therapeutic immunity to antigen-expressing tumors. Thus, OmpA belongs to a class of proteins that are able to elicit CTL responses to exogenous antigen.

L12 ANSWER 3 OF 4 MEDLINE on STN
AN 90361436 MEDLINE
TI Interleukin-6 gene expression and production induced in human monocytes by membrane proteoglycans from Klebsiella pneumoniae.
AU Sironi M; Sica A; Riganti F; Licciardello L; Colotta F; Mantovani A
SO INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1990) 12 (4) 397-402.

Journal code: 7904799. ISSN: 0192-0561.

AB The present study was designed to investigate the effect of membrane proteoglycans (MPG) from Klebsiella pneumoniae on IL-6 production by human peripheral blood monocytes. Exposure in vitro to MPG induced release of IL-6 activity from human monocytes, as assessed by the 7TD1 hybridoma assay. MPG-induced hybridoma growth factor activity was blocked by anti-IL-6 antibodies. MPG induced expression in human monocytes of IL-6 mRNA transcripts as assessed by Northern blot analysis. Induction of IL-6 in mononuclear phagocytes may play a role in the immunomodulatory activity of MPG.

L12 ANSWER 4 OF 4 MEDLINE on STN
AN 90116958 MEDLINE
TI Polyclonal B-cell activation by bacteria that induce nonsuppurative sequelae.
AU Gross W L
SO RHEUMATOLOGY INTERNATIONAL, (1989) 9 (3-5) 205-11. Ref: 28
Journal code: 8206885. ISSN: 0172-8172.
AB The polyclonal B cell activation (PBA) process induced by Klebsiella pneumoniae K34 (klebs) and Yersinia enterocolitica 03 (yers) was investigated. Both heat-inactivated bacteria and their cell wall biostructures (klebsM, muriene, protein I etc.) stimulate human blood B cells to differentiate into immunoglobulin-secreting cells without prior proliferation and without T cells. Klebs-activated B cells secrete mainly IgM and to a lesser degree IgG (mainly IgG2). The PBA process was regulated by CD4+ cells and monocytes, but not by CD8+ cells. While interleukin 2 is able both to induce proliferation and to enhance differentiation in klebs-activated B cell cultures, the low-molecular-weight B cell growth factor (BCGF) did not lead to a significant amount of 3H-thymidine uptake. In addition, in klebs-activated B cell cultures various anti-polynucleotide autoantibodies and the 16/6 idiotype were detectable. Thus, bacteria that induce nonsuppurative sequelae (e.g. klebs, yers) can use several mechanisms to overcome tolerance in their host.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, CANCERLIT' ENTERED AT 12:26:15 ON 07 AUG 2003)

-Author (s)

L13	999	SEA ABB=ON	PLU=ON	"BONNEFOY J"?/AU
L14	8	SEA ABB=ON	PLU=ON	"LECOANET S"?/AU
L15	1343	SEA ABB=ON	PLU=ON	("AUBRY J"? OR "AURBY J"?)/AU
L16	592	SEA ABB=ON	PLU=ON	("PASCALE J"? OR "JEANNIN P"?)/AU
L17	160	SEA ABB=ON	PLU=ON	"BAUSSANT T"?/AU
L18	3	SEA ABB=ON	PLU=ON	L13 AND L14 AND L15 AND L16 AND L17
L19	418	SEA ABB=ON	PLU=ON	L13 AND (L14 OR L15 OR L16 OR L17)
L20	8	SEA ABB=ON	PLU=ON	L14 AND (L15 OR L16 OR L17)
L21	80	SEA ABB=ON	PLU=ON	L15 AND (L16 OR L17)
L22	21	SEA ABB=ON	PLU=ON	L16 AND L17
L23	78	SEA ABB=ON	PLU=ON	(L19 OR L21 OR L13 OR L14 OR L15 OR L16 OR L17) AND (L1 OR L2)
L24	86	SEA ABB=ON	PLU=ON	L18 OR L20 OR L22 OR L23
L25	30	DUP REM L24	(56 DUPLICATES REMOVED)	

L25 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:192820 HCAPLUS
DOCUMENT NUMBER: 138:203652
TITLE: Use of low-molecular-weight enterobacterial Omp

as a carrier and/or adjuvant
INVENTOR(S): **Jeannin, Pascale**; Libon, Christine; **Baussant, Thierry**; Haeuw, Jean Francois; Gauchat, Jean Francois
PATENT ASSIGNEE(S): Pierre Fabre Medicament S. A., Fr.
SOURCE: Fr. Demande, 39 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2828106	A1	20030207	FR 2001-10381	20010802

PRIORITY APPLN. INFO.: FR 2001-10381 20010802

AB The invention concerns a pharmaceutical compn. comprising, in a pharmaceutically acceptable medium, ant least one peptide coming from a low-mol.-wt. enterobacterial Omp (outer membrane protein) or a nucleic acid coding for said peptide. The peptide or nucleic acid construct may be used to prep. a vaccine intended for treatment or prophylaxis against viral, bacterial, or fungal infections or parasitism, and may be used in prevention and treatment of cancers.

L25 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:137763 HCAPLUS
DOCUMENT NUMBER: 138:186095
TITLE: **Outer membrane protein A** renders dendritic cells and macrophages responsive to CCL21 and triggers dendritic cell migration to secondary lymphoid organs
AUTHOR(S): **Jeannin, Pascale**; Magistrelli, Giovanni; Herbault, Nathalie; Goetsch, Liliane; Godefroy, Sylvie; Charbonnier, Peggy; Gonzalez, Alexandra; Delneste, Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, Fr.
SOURCE: European Journal of Immunology (2003), 33(2), 326-333
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Outer membrane protein A** (**OmpA**) is a class of bacterial cell wall protein that is immunogenic without adjuvant. As specific immune responses are initiated in the lymph nodes (LN), the authors analyzed the effect of the **OmpA** from **Klebsiella pneumoniae** (**KpOmpA**) on chemokine/chemokine receptor expression by APC and on cell migration to the LN. Upon contact with **KpOmpA**, human immature DC and macrophages acquire CCR7 expression and responsiveness to CCL21. In parallel, CCR1 and CCR5 expression is down-regulated and CXCL8, CCL2, CCL3 and CCL5 prodn. is up-regulated. Mice injected s.c. with **KpOmpA** present a transient inflammatory reaction at the site of injection accompanied by an enlargement of the draining LN with a higher proportion of DC and macrophages. Lastly, when exposed to **KpOmpA** prior

injection, DC but not macrophages migrate to the draining LN. In conclusion, **KpOmpA** confers a migratory phenotype to DC and triggers their migration to the regional LN. This property contributes to explain how innate cells initiate adaptive immune response upon recognition of conserved bacterial components and also why **OmpA** is immunogenic in the absence of adjuvant.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:515586 HCAPLUS

TITLE: **Outer membrane protein A (OmpA)** activates human epidermal Langerhans cells

AUTHOR(S): Godefroy, Sylvie; Corvaia, Nathalie; Schmitt, Daniel; **Aubry, Jean-Pierre; Bonnefoy, Jean-Yves; Jeannin, Pascale**; Staquet, Marie-Jeanne

CORPORATE SOURCE: Hopital E. Herriot, INSERM U346, affilie CNRS, Lyon, Fr.

SOURCE: European Journal of Cell Biology (2003), 82(4), 193-200
CODEN: EJCBDN; ISSN: 0171-9335

PUBLISHER: Urban & Fischer Verlag GmbH & Co. KG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Outer membrane protein (**Omp**)**A** is highly represented and conserved in the **Enterobacteriaceae** family. Using a recombinant **OmpA** from **Klebsiella pneumoniae** (**kpOmpA**), we have analyzed the interaction between this bacterial cell wall protein and human Langerhans cells (LC), the antigen-presenting cells of the epidermis and mucosa. We showed that biotinylated **kpOmpA** binds to human LC freshly isolated from epidermis. **KpOmpA** up-regulated MHC class II, CD86 and CCR7 expression, enhanced migration in response to macrophage inflammatory protein-3.beta. (MIP-3.beta.) through a reconstituted basement membrane mimicking the prerequisite passage through the dermal-epidermal basement membrane on the way to lymph nodes. The allostimulatory function of **kpOmpA**-treated LC was more potent than that of untreated cells. Even though the proportion of LC which binds **kpOmpA** was shown to vary between individuals, our data indicate that **kpOmpA** binds to and activates LC, and suggest that recognition of **OmpA** by LC may be an initiating event in the antibacterial host response.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2002:357107 HCAPLUS

DOCUMENT NUMBER: 137:293167

TITLE: Streptococcus pneumoniae polysaccharides conjugated to the **outer membrane protein A** from **Klebsiella pneumoniae** elicit protective antibodies

AUTHOR(S): Libon, Christine; Haeuw, Jean Francois; Crouzet, Francoise; Mugnier, Chantal; **Bonnefoy, Jean Yves**; Beck, Alain; Corvaia, Nathalie
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, St. Julien en Genevois, 74164, Fr.
SOURCE: Vaccine (2002), 20(17-18), 2174-2180
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polysaccharides (PSs) derived from S. pneumoniae include >90 serotypes and differ greatly in their immunogenicity. In addn., immunization with PSs does not induce high affinity antibody prodn. and no memory B-cells are generated. Coupling PSs to carrier proteins has been reported to induce B-cell maturation and to install a B-cell memory. As an alternative carrier protein, the **outer membrane protein A** (**OmpA**) derived from **K. pneumoniae** has been coupled to various PSs. The authors evaluated the immunogenicity of 2 PS conjugates, using PS derived from S. pneumoniae types 14 and 19, resp. Here, they show that anti-PS IgG responses are generated after the conjugation of PSs to P40. In addn., the humoral response generated is able to protect mice from a bacterial challenge. Thus, P40 could be included in the development of new PS conjugate vaccines.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2002:930988 HCAPLUS
DOCUMENT NUMBER: 138:185779
TITLE: **Outer membrane protein A (OmpA)**: a new pathogen-associated molecular pattern that interacts with antigen presenting cells-impact on vaccine strategies
AUTHOR(S): **Jeannin, Pascale**; Magistrelli, Giovanni; Goetsch, Liliane; Haeuw, Jean-Francois; Thieblemont, Nathalie; **Bonnefoy, Jean-Yves**; Delneste, Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.
SOURCE: Vaccine (2002), 20(Suppl. 4), A23-A27
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. **Outer membrane protein A (OmpA)** is a class of proteins highly conserved among the **Enterobacteriaceae** family and throughout evolution. The authors have obsd. that antigen presenting cells (APCs) recognize and are activated by the recombinant **OmpA** from **Klebsiella pneumoniae** (**KpOmpA**). **KpOmpA** triggers cytokine prodn. by macrophages and dendritic cells (DC), induces DC maturation and signals via Toll-like receptor 2. **KpOmpA** also interacts with endocytic receptor(s) expressed on DC and macrophages. Tumor antigens coupled to

KpOmpA are taken up by APCs and gain access to the MHC class I pathway, triggering the initiation of protective anti-tumor cytotoxic responses in the absence of CD4 T cell help and adjuvant. Thus, **OmpA** appears as a new type of pathogen-assocd. mol. pattern (PAMP) usable as a vector in anti-infectious and therapeutic anti-tumor vaccines to elicit CTLs.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:850960 HCAPLUS
DOCUMENT NUMBER: 136:582
TITLE: Use of an **enterobacterial OmpA** protein as antimicrobial agent
INVENTOR(S): **Jeannin, Pascale**; Delneste, Yves; **Baussant, Thierry**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087326	A1	20011122	WO 2001-FR1490	20010516
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
FR 2809014	A1	20011123	FR 2000-6199	20000516

PRIORITY APPLN. INFO.: FR 2000-6199 A 20000516

AB The invention concerns the use of an **enterobacterium OmpA** protein or one of its fragments, in particular of **Klebsiella pneumoniae**, as an antimicrobial agent or for prepg. an antimicrobial pharmaceutical compn. for mucosal delivery. The invention further concerns said compns., preferably antigen-free, and a device adapted for mucosal delivery characterized in that it contains the inventive compn.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2001:816483 HCAPLUS
DOCUMENT NUMBER: 135:352772
TITLE: Omp protein associated with autologous and/or heterologous tumor cell lysate
INVENTOR(S): Renno, Toufic; Invernizzi, Isabelle; **Bonnefoy, Jean-Yves**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082959	A1	20011108	WO 2001-FR1348	20010503
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
FR 2808445	A1	20011109	FR 2000-5702	20000504
EP 1278539	A1	20030129	EP 2001-931780	20010503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: FR 2000-5702 A 20000504
WO 2001-FR1348 W 20010503

AB The invention concerns a pharmaceutical compn. comprising an Omp membrane protein, in particular an **OmpA** membrane protein of **Klebsiella pneumoniae**, assocd. with lysate of autologous and/or heterologous tumor cells and the use of said compns. for preventing and treating cancer. The invention also concerns a method for isolating tumor antigens using said Omp. Antitumoral activity of P40 protein in guinea pigs was shown.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2001:507718 HCAPLUS
DOCUMENT NUMBER: 135:106360
TITLE: Solubilization of proteins for antigen use in an aqueous solvent without using detergents
INVENTOR(S): **Baussant, Thierry; Jeannin, Pascale**; Delneste, Yves; Lawny, Francois; **Bonnefoy, Jean-Yves**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049705	A2	20010712	WO 2001-FR23	20010104
WO 2001049705	A3	20020214		
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
FR 2803302	A1	20010706	FR 2000-70	20000104
EP 1244690	A2	20021002	EP 2001-903868	20010104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001007421	A	20021022	BR 2001-7421	20010104
JP 2003519238	T2	20030617	JP 2001-550245	20010104
US 2003044915	A1	20030306	US 2002-169953	20020703

PRIORITY APPLN. INFO.: FR 2000-70 A 20000104
WO 2001-FR23 W 20010104

AB The invention concerns a novel method for prepg. a polypeptide sol. in an aq. solvent in the absence of detergent, and polypeptides

obtainable by said method. The invention also concerns the use of said polypeptides, in particular for prepg. medicines or vaccines, against bacterial and viral infections or cancers. Specifically, the method is used for hydrophobic membrane proteins such as porins to allow them to be used in vaccines without the use of detergents. The **ompA** porin (rP40) of **Klebsiella pneumoniae** was manufd. by expression of the cloned gene in EScherichia coli where it accumulated as inclusion bodies. The inclusion bodies were recovered from lysates by centrifugation and solubilized in urea 7M, dithiothreitol 10 mM, Tris HCl (25 mM, pH 8.5) at 37.degree. for 2h. The solubilized material was dild. with 13 vols. of NaCl (8.76 g/L), Zwittergent 3-14 (0.1 vol%), Tris HCl (25 mM, pH 8.5) and allowed to renature overnight at room temp. and desalted by dialysis against Tris HCl (25 mM, pH 8.5), Zwittergent 3-14 (0.1 vol%) at 4.degree.. The dialyzed material was purified by ion-exchange chromatog. against strong anion and cation exchangers to yield a protein solubilized with Zwittergent 3-14. The purified protein was pptd. with 5 vols. of ethanol, resolubilized in urea 7M as before to yield a stable hydrophilic form that was predominantly .alpha.-helical as opposed to the hydrophilic .beta.-sheet protein. The protein was able to induce CD38 synthesis and interleukin 12 secretion in human dendritic cells. The effects were polymyxin B sensitive and therefore not due to contaminating endotoxins.

L25 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2001:569802 HCAPLUS
DOCUMENT NUMBER: 135:179693
TITLE: Denaturation, solubilization and renaturation of proteins for use in nasal vaccines
INVENTOR(S): Andreoni, Christine; Rauly, Isabelle; N'Guyen, Thien; Haeuw, Jean Francois; **Baussant, Thierry**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: Fr. Demande, 48 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2801219	A1	20010525	FR 2000-11862	20000918
PRIORITY APPLN. INFO.:			FR 2000-11862	20000918

AB Methods of solubilizing and renaturing proteins for use in vaccines, esp. for nasal delivery, are described. Specifically, the p40 **ompA** protein of **Klebsiella pneumonia** is purified. The protein was manufd. by expression of the cloned gene in Escherichia coli where it accumulated as inclusion bodies (10% of bacterial dry wt.). Inclusion bodies were denatured in urea 7M, Tris HCl (25 mM, pH8.5), dithiothreitol 10 mM at 37.degree. for 2h and dild. with a 13 vols. of a soln. of NaCl (8.7 g/L), Zwittergent 3-14 (0.1 vol%). The solubilized proteins were purified by fractionation on strong anion- and cation-exchangers before being coupled to an antigenic peptide of protein G of respiratory syncytial virus. Mice that had been presensitized to **Klebsiella pneumoniae** were given the protein conjugate intranasally. After a booster administration, the mice

presented antibodies to the p40 protein and the G protein peptide. These were IgA mols. typically found in response to oronasal infection.

L25 ANSWER 10 OF 30 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-427232 [46] WPIDS
DOC. NO. CPI: C2001-129432
TITLE: Preparing purified polypeptide soluble in absence of detergent, useful for modulating the immune system, e.g. in vaccines, by removal of detergent, denaturing and molecular sieving.
DERWENT CLASS: B04 D16
INVENTOR(S): **BAUSSANT, T; BONNEFOY, J;** DELNESTE, Y; **JEANNIN, P;** LAWNY, F; **BONNEFOY, J Y;** JHEANNIN, P
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE; (BAUS-I) BAUSSANT T; (BONN-I) BONNEFOY J; (DELN-I) DELNESTE Y; (JEAN-I) JEANNIN P; (LAWN-I) LAWNY F
COUNTRY COUNT: 34
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2803302	A1	20010706	(200146)*		34
WO 2001049705	A2	20010712	(200146)	FR	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU BR CA CN JP MX US ZA					
AU 2001031837	A	20010716	(200169)		
EP 1244690	A2	20021002	(200265)	FR	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
BR 2001007421	A	20021022	(200278)		
US 2003044915	A1	20030306	(200320)		
ZA 2002004930	A	20030430	(200334)		77
CN 1396927	A	20030212	(200335)		
JP 2003519238	W	20030617	(200349)		45

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2803302	A1	FR 2000-70	20000104
WO 2001049705	A2	WO 2001-FR23	20010104
AU 2001031837	A	AU 2001-31837	20010104
EP 1244690	A2	EP 2001-903868	20010104
		WO 2001-FR23	20010104
BR 2001007421	A	BR 2001-7421	20010104
		WO 2001-FR23	20010104
US 2003044915	A1	WO 2001-FR23	20010104
		US 2002-169953	20020703
ZA 2002004930	A	ZA 2002-4930	20020619
CN 1396927	A	CN 2001-804096	20010104
JP 2003519238	W	JP 2001-550245	20010104
		WO 2001-FR23	20010104

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2001031837	A	Based on	WO 200149705
EP 1244690	A2	Based on	WO 200149705
BR 2001007421	A	Based on	WO 200149705
JP 2003519238	W	Based on	WO 200149705

PRIORITY APPLN. INFO: FR 2000-70 20000104
AN 2001-427232 [46] WPIDS
AB FR 2803302 A UPAB: 20010815

NOVELTY - Preparation (M1) of a purified solution of a polypeptide (I) that is soluble in aqueous solvent in absence of detergent (II), comprising:

(i) removing (II);

(ii) solubilizing (I) in solution of denaturing agent; and

(iii) eluting, in aqueous solution, soluble (I) by molecular sieving column chromatography, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) water-soluble (I) produced by M1;

(b) modulating the immune system in mammals towards an antigen by inducing maturation of isolated dendritic cells (DC) in the presence of (I); and

(c) modulating the immune system in a mammal by injecting (I), alone or as adjuvant.

ACTIVITY - Immunomodulatory; immunostimulatory; antiviral; anti-human immunodeficiency virus; antibacterial; anticancer; antimycotic; antifungal; antiparasitic; cardiant; anti-inflammatory.

MECHANISM OF ACTION - Vaccine. The preferred (I), **outer membrane protein A** (P40) of **Klebsiella pneumoniae**, binds selectively to antigen-presenting cell, so provides targeting, proliferation and/or expression of molecules by these cells. Recombinant soluble P40 was conjugated to ovalbumin and the composition used to inject mice. Spleen cells were incubated with irradiated E.G7 cells and then tested (as effector) against chromium-labeled target cells (EL4, pulsed with E.G7 and the peptide SIINFEKL). Specific lysis at effector:target ratio 100:1 was 40%, comparable with that for a conjugate of non-solubilized P40.

USE - (I) are used, alone or as an adjuvant, to produce therapeutic compositions that are soluble in absence of (II), especially when formulated with an antigen or hapten (A) for modulating the host's immune system. Especially they are used to prepare vaccines, especially antiviral, antibacterial or anticancer (e.g. against human immune deficiency virus, respiratory syncytial virus, measles, mumps, tuberculosis etc.), but also (not claimed) against fungi, parasites, autoimmune diseases, graft rejection, cardiovascular disease, inflammation and immune deficiency.

ADVANTAGE - (I) can be administered without co-injection of potentially harmful detergents, and may have an altered tertiary structure that affects biological activity, particularly causing an alteration that renders (I) hydrophilic. They are particularly useful for use with weakly immunogenic antigens or haptens.

Dwg.0/6

L25 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2001:714059 HCAPLUS
DOCUMENT NUMBER: 136:18965
TITLE: Targeting of nasal mucosa-associated

antigen-presenting cells in vivo with an **outer membrane protein A** derived from **Klebsiella pneumoniae**

AUTHOR(S): Goetsch, Liliane; Gonzalez, Alexandra; Plotnicky-Gilquin, Helene; Haeuw, Jean Francois; **Aubry, Jean Pierre**; Beck, Alain; **Bonnefoy, Jean Yves**; Corvaia, Nathalie

CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, 74164, Fr.

SOURCE: Infection and Immunity (2001), 69(10), 6434-6444
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Administration of vaccines by the nasal route has recently proven to be one of the most efficient ways for inducing both mucosal and systemic antibody responses in exptl. animals. Our results demonstrate that P40, a well-defined **outer membrane protein A** from **Klebsiella pneumoniae**, is indeed a carrier mol. suitable for nasal immunization. Using fragments from the respiratory syncytial virus subgroup A (RSV-A) G protein as antigen models, it has been shown that P40 is able to induce both systemic and mucosal immunity when fused or coupled to a protein or a peptide and administered intranasally (i.n.) to naive or **K. pneumoniae**-primed mice. Confocal analyses of nasal mucosa-assocd. lymphoid tissue after i.n. instillation of P40 showed that this mol. is able to cross the nasal epithelium and target CD11c-pos. cells likely to be murine dendritic cells or macrophages. More importantly, this targeting of antigen-presenting cells following i.n. immunization with a subunit of the RSV-A mol. in the absence of any mucosal adjuvant results in both upper and lower respiratory tract protection against RSV-A infection.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2002:127710 HCAPLUS

DOCUMENT NUMBER: 137:61733

TITLE: Stability and CTL-activity of P40/ELA melanoma vaccine candidate

AUTHOR(S): Beck, A.; Goetsch, L.; Champion, T.; Bussat, M.-C.; **Aubry, J.-P.**; Klinguer-Hamour, C.; Haeuw, J.-F.; **Bonnefoy, J.-Y.**; Corvaia, N.

CORPORATE SOURCE: BioMerieux-Pierre Fabre, Centre d'Immunologie Pierre Fabre (CIPF), Saint-Julien-en-Genevois, F-74164, Fr.

SOURCE: Biologicals (2001), 29(3/4), 293-298
CODEN: BILSEC; ISSN: 1045-1056

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The decapeptide ELA (ELAGIGILTV), a Melan-A/MART-1 antigen immunodominant peptide analog, is an interesting melanoma vaccine candidate alone or in combination with other tumor antigens. P40,

the recombinant **outer membrane protein A** of **Klebsiella pneumoniae** (**kpOmpA**), was recently shown to target dendritic cells and to induce peptide-specific CTLs. Here the authors investigated the adjuvant role of P40 mixed or chem. conjugated to ELA. This compd. is an N-terminal glutamic acid-contg. peptide.. However, it has been reported that the amino group and the .gamma.-carboxylic group of glutamic acids easily condense to form pyroglutamic derivs. Usually, to overcome this stability problem, peptides of pharmaceutical interest were developed with a pyroglutamic acid instead of N-terminal glutamic acid, without loss of pharmacol. properties. Unfortunately, the pyroglutamic acid deriv. (PyrELA) as well as the N-terminal acetyl capped deriv. (AcELA) failed to elicit CTL activity when mixed with P40 adjuvant protein. Despite the apparent minor modifications introduced by PyrELA and AcELA, these two derivs. have probably lower affinity than ELA for the class 1 Major Histocompatibility Complex. Furthermore, this stability problem is worse in the case of clin. grade ELA, produced as an acetate salt, like most of the pharmaceutical grade peptides. The authors report here that the hydrochloride shows a higher stability than the acetate and may be suitable for use in man. (c) 2001 The International Association of Biological Standardization.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2000:608604 HCAPLUS
DOCUMENT NUMBER: 133:213048
TITLE: Protein **OmpA** of **Klebsiella pneumoniae** associated with the human chorionic gonadotropin hormone or a compound involved in cell proliferation or fertility
INVENTOR(S): Goetsch, Liliane; Corvaia, Nathalie; Beck, Alain; Haeuw, Jean-Francois; **Bonnefoy, Jean-Yves**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050071	A1	20000831	WO 2000-FR463	20000224
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2789902	A1	20000825	FR 1999-2314	19990224

PRIORITY APPLN. INFO.: FR 1999-2314 A 19990224

AB The invention concerns the use of a mixt. or complex comprising an **enterobacterium** membrane protein **OmpA**, in particular of **Klebsiella pneumoniae**, assocd. with an immunogen selected among the .beta.hCG, a compd. involved in tumor cell proliferation or fertility, or with one of their fragments, for prepg. a pharmaceutical compn. for enhancing the

response against said immunogen. The invention further concerns a pharmaceutical compn. comprising said mixt. or complex in particular for preventing and for treating tumors, or for treating fertility.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 2000:592579 HCAPLUS
DOCUMENT NUMBER: 133:191985
TITLE: Use of an **OmpA enterobacterium** protein associated with the ELAGIGILTV peptide for treating melanomas
INVENTOR(S): Renno, Toufic; Romero, Pedro; Miconnet, Isabelle; Carottini, Jean-Charles; **Bonnefoy, Jean-Yves**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048629	A1	20000824	WO 2000-FR394	20000217
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2789588	A1	20000818	FR 1999-1917	19990217
FR 2789588	B1	20010504		
EP 1150707	A1	20011107	EP 2000-906412	20000217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 2000008305	A	20020122	BR 2000-8305	20000217
JP 2003506315	T2	20030218	JP 2000-599419	20000217
ZA 2001006800	A	20020510	ZA 2001-6800	20010817

PRIORITY APPLN. INFO.: FR 1999-1917 A 19990217
WO 2000-FR394 W 20000217

AB The invention concerns the use of an **enterobacterium** membrane protein **OmpA**, in particular of **Klebsiella pneumoniae** , assocd. with an antigen or a hapten for prepg. a pharmaceutical compn. designed to generate or enhance a cytotoxic T response directed against a tumor cell. The invention also concerns the use of said compds. for preventing or treating infection or cancer, in particular cancers assocd. with a tumoral antigen such as melanoma, and pharmaceutical compns. comprising some of said compds.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 14
ACCESSION NUMBER: 2000:592578 HCAPLUS
DOCUMENT NUMBER: 133:191984
TITLE: Use of an **enterobacterium** protein **OmpA** associated with an antigen for

generating an antiviral, antiparasitic, or antitumoral cytotoxic response
INVENTOR(S): Renno, Toufic; **Bonnefoy, Jean-Yves**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048628	A1	20000824	WO 2000-FR393	20000217
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2789588	A1	20000818	FR 1999-1917	19990217
FR 2789588	B1	20010504		
EP 1150706	A1	20011107	EP 2000-906411	20000217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 2000008307	A	20020122	BR 2000-8307	20000217
JP 2003506314	T2	20030218	JP 2000-599418	20000217
ZA 2001006800	A	20020510	ZA 2001-6800	20010817

PRIORITY APPLN. INFO.: FR 1999-1917 A 19990217
WO 2000-FR393 W 20000217

AB The invention concerns the use of an **enterobacterium OmpA** membrane protein, in particular of **Klebsiella pneumoniae** assocd. with an antigen or a hapten for prepg. a pharmaceutical compn. for generating or enhancing a cytotoxic T response directed against an infectious or tumor cell. The invention also concerns the use of said compds. for preventing and treating infection or cancer, in particular cancers assocd. with a tumoral antigen such as melanoma, and pharmaceutical compns. comprising some of said compds.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 15
ACCESSION NUMBER: 2000:335272 HCAPLUS
DOCUMENT NUMBER: 132:352759
TITLE: Use of an **OmpA** outer membrane protein of an **enterobacterium** for specific targeting of drugs to antigen-presenting cells
INVENTOR(S): **Bonnefoy, Jean-Yves; Lecoanet, Sybille; Aubry, Jean-Pierre; Jeannin, Pascale; Baussant, Thierry**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027432	A1	20000518	WO 1999-FR2734	19991108
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2785542	A1	20000512	FR 1998-14007	19981106
FR 2785542	B1	20010209		
BR 9915071	A	20010717	BR 1999-15071	19991108
EP 1124577	A1	20010822	EP 1999-971719	19991108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002529428	T2	20020910	JP 2000-580661	19991108

PRIORITY APPLN. INFO.: FR 1998-14007 A 19981106
WO 1999-FR2734 W 19991108

AB The invention concerns the use of an **enterobacterium** protein **OmpA**, preferably **Klebsiella pneumoniae** P40 protein, for specific targeting of a biol. active substance assocd. therewith towards antigen-presenting cells, in particular human dendritic cells. The invention also concerns the use of the **OmpA** protein for prepg. a pharmaceutical compn. for preventing and/or treating diseases, in particular cancers related to a tumor-assocd. antigen, autoimmune diseases or infectious diseases. The protein can be manufd. as inclusion bodies in Escherichia coli and purified chromatog. after solubilization. Alexa 488-labeled **K. pneumoniae OmpA** (p40) showed specific, dose-dependent binding to dendritic cells. Other possible carrier proteins, such as tetanus toxins and protein G derivs. did not bind dendritic cells. P40 is also internalized by dendritic cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 30 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-573921 [54] WPIDS
DOC. NO. CPI: C2000-171201
TITLE: Use of **enterobacterial** outer membrane protein as immunogenic carrier, particularly for contraceptive and anti-cancer vaccines, provides strong humoral response.
DERWENT CLASS: B04 D16
INVENTOR(S): BECK, A; **BONNEFOY, J Y**; CORVAIA, N; GOETSCH, L; HAEUW, J F; **BONNEFOY, J**; HAEUW, J
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2789902	A1	20000825	(200054)*		34
WO 2000050071	A1	20000831	(200054)	FR	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CN JP MX US ZA					
AU 2000029211	A	20000914	(200063)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2789902	A1	FR 1999-2314	19990224
WO 2000050071	A1	WO 2000-FR463	20000224
AU 2000029211	A	AU 2000-29211	20000224

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000029211	A	Based on	WO 200050071

PRIORITY APPLN. INFO: FR 1999-2314 19990224
AN 2000-573921 [54] WPIDS
AB FR 2789902 A UPAB: 20001027
NOVELTY - Use of an **enterobacterial outer membrane protein A** (**OmpA**), or its fragments, associated with an immunogen (I), to prepare a pharmaceutical composition for improving the immunological response to (I). (I) is at least one of cytokine, growth factor or hormone (or their receptors) and/or tumor-specific markers, or their fragments or analogs.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) pharmaceutical composition containing **OmpA**, or its fragments, particularly from **Klebsiella pneumoniae**, associated with, as immunogen, a cytokine, growth factor and/or hormone, or their fragments; and

(b) pharmaceutical composition containing a nucleic acid construct encoding **OmpA**, as in (a), associated with a nucleic acid encoding an immunogenic peptide as in (a).

ACTIVITY - Antitumor; contraceptive.

Mice were injected (subcutaneously at the base of the neck) with a conjugate of **OmpA** from **K. pneumoniae** and a human chorionic gonadotrophin peptide, formulated with the adjuvants N-acertylmuramyl-L-alanyl-D-isoglutamine and squalene mannoside mono-oleate. Four injections were given (days 0, 7, 14, 22) and antibody titers measured on days 7, 14, 22 and 35. At doses of 0.1 mg conjugate, the anti-peptide titer (log10) on day 35 was over 5; even with a dose of 1 micro g it was over 4.

MECHANISM OF ACTION - Induction of a specific immune response.

USE - Compositions containing (I) and **OmpA** are especially useful in vaccines (i) to prevent or treat cancer or (ii) as contraceptives.

ADVANTAGE - Compositions containing **OmpA** and (I) induce a strong and specific antibody response against (I), beginning with the second injection, and cause a significantly greater reduction in tumor mass than similar vaccines containing diphtheria toxin as carrier. They do not require an additional adjuvant.

Dwg.0/7

L25 ANSWER 18 OF 30 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:357252 BIOSIS
DOCUMENT NUMBER: PREV200100357252

TITLE: Physico-chemical characterization and immunogenicity studies of peptide and polysaccharide conjugate vaccines based on a promising new carrier protein, the recombinant **Klebsiella pneumoniae OmpA.**

AUTHOR(S): Haeuw, J. F. (1); Libon, C. (1); Zanna, L. (1); Goetsch, L. (1); Champion, T. (1); Nguyen, T. N. (1); **Bonnefoy, J. Y. (1)**; Corvaia, N. (1); Beck, A. (1)

CORPORATE SOURCE: (1) Centre d'Immunologie Pierre Fabre, Saint-Julien-en-Genevois France

SOURCE: Brown, F.; Corbel, Michael J.; Griffiths, Elwyn. Developments in Biologicals, (2000) Vol. 103, pp. 245-250. Developments in Biologicals. Physico-chemical procedures for the characterization of vaccines. print.
Publisher: S. Karger Publishers Inc. 79 Fifth Avenue, New York, NY, 10003, USA.
Meeting Info.: Meeting on Physico-Chemical Procedures for the Characterization of Vaccines France December 01-03, 1999
ISSN: 1424-6074. ISBN: 3-8055-7101-1 (paper).

DOCUMENT TYPE: Book; Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 2000:617836 HCAPLUS
DOCUMENT NUMBER: 133:295209

TITLE: Cutting edge: **outer membrane protein A (OmpA)** binds to and activates human macrophages

AUTHOR(S): Soulas, Caroline; **Baussant, Thierry**; **Aubry, Jean-Pierre**; Delneste, Yves; Barillat, Nicolas; Caron, Gersende; Renno, Toufic; **Bonnefoy, Jean-Yves**; **Jeannin, Pascale**

CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.

SOURCE: Journal of Immunology (2000), 165(5), 2335-2340
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **OmpA** is highly represented and conserved in the **Enterobacteriaceae** family. Using a recombinant **OmpA** from **Klebsiella pneumoniae** (P40), the authors analyzed the interaction between **OmpA** and macrophages. They report that Alexa488-labeled P40 binds (at 4.degree.) to murine and human macrophages in a dose-dependent manner and is rapidly internalized (at 37.degree.). No binding or internalization of the Alexa488-labeled glycophorin A control protein is obsd. under the same conditions. Furthermore, P40 up-regulates the prodn. of IL-1.beta., IL-8, IL-10, IL-12, and TNF-.alpha. by human macrophages and of NO by the RAW 264.7 murine macrophage cell line. P40 also synergizes with IFN-.gamma. and suboptimal concns. of LPS to up-regulate the prodn. of these mediators. Thus, P40 binds to and activates macrophages. It is suggested that recognition of

OmpA by macrophages may be an initiating event in the antibacterial host response.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 17
ACCESSION NUMBER: 2000:878892 HCAPLUS
DOCUMENT NUMBER: 134:146071
TITLE: **OmpA** targets dendritic cells, induces their maturation and delivers antigen into the MHC class I presentation pathway
AUTHOR(S): **Jeannin, Pascale**; Renno, Toufic; Goetsch, Liliane; Miconnet, Isabelle; **Aubry, Jean-Pierre**; Delneste, Yves; Herbault, Nathalie; **Baussant, Thierry**; Magistrelli, Giovanni; Soulas, Caroline; Romero, Pedro; Cerottini, Jean-Charles; **Bonnefoy, Jean-Yves**
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.
SOURCE: Nature Immunology (2000), 1(6), 502-509
CODEN: NIAMCZ; ISSN: 1529-2908
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors analyzed the interaction between a bacterial cell wall protein and dendritic cells (DCs). **Outer membrane protein A** from **Klebsiella pneumoniae** (**kpOmpA**) specifically bound to professional antigen presenting cells and was endocytosed by immature DCs via a receptor-dependent mechanism. **KpOmpA** signaled through Toll-like receptor 2, induced DCs to produce interleukin 12 and induced maturation of DCs. Whole antigen that was coupled to **kpOmpA** and injected into mice was taken up by DCs and delivered to the conventional cytosolic MHC class I presentation pathway. **KpOmpA** also primed antigen-specific CD8+ CTLs in the absence of CD4+ T cell help or adjuvant and elicited therapeutic immunity to antigen-expressing tumors. Thus, **OmpA** belongs to a class of proteins that are able to elicit CTL responses to exogenous antigen.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 18
ACCESSION NUMBER: 2001:75670 HCAPLUS
DOCUMENT NUMBER: 135:120947
TITLE: Physicochemical characterization and immunogenicity studies of peptide and polysaccharide conjugate vaccines based on a promising new carrier protein, the recombinant **Klebsiella pneumoniae OmpA**
AUTHOR(S): Haeuw, J. F.; Libon, C.; Zanna, L.; Goetsch, L.; Champion, T.; Nguyen, T. N.; **Bonnefoy, J. Y.**; Corvaia, N.; Beck, A.
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre,

Saint-Julien-en-Genevois, Fr.
SOURCE: Developments in Biologicals (Basel, Switzerland) (2000), 103(Physico-Chemical Procedures for the Characterization of Vaccines), 245-250
CODEN: DBEIAI; ISSN: 1424-6074
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The recombinantly expressed and refolded **K. pneumoniae OmpA**, called rP40, has been previously shown to be identical to the native form purified from **K. pneumoniae** from structural and immunol. points of view. An efficient procedure has been developed for obtaining large quantities of rP40. Using various anal. methods, the structural integrity of the purified protein was demonstrated. When conjugated to peptides and polysaccharides and used to immunize animals, rP40 exerts a powerful carrier effect facilitating the induction of peptide or polysaccharide antibodies. The antibody responses generated after P40 conjugates administration are equiv. to those obtained after immunization with the ref. carrier tetanus toxoid coupled to the same antigens. Data from preclin. studies suggest that rP40 would be an excellent carrier protein for human conjugate vaccines.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:640730 HCAPLUS
DOCUMENT NUMBER: 131:291268
TITLE: Use of active P40 conjugates for immunostimulant nasal delivery
INVENTOR(S): Andreoni, Christine; Rauly, Isabelle; N'guyen, Thien; Haeuw, Jean-francois; **Baussant, Thierry**
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949892	A2	19991007	WO 1999-FR703	19990326
WO 9949892	A3	20000330		
W: AU, BR, CA, CN, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2776521	A1	19991001	FR 1998-3814	19980327
FR 2776521	B1	20001215		
CA 2324477	AA	19991007	CA 1999-2324477	19990326
AU 9929391	A1	19991018	AU 1999-29391	19990326
BR 9909180	A	20001205	BR 1999-9180	19990326
EP 1066054	A2	20010110	EP 1999-910434	19990326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2002509897 T2 20020402 JP 2000-540854 19990326
PRIORITY APPLN. INFO.: FR 1998-3814 A 19980327
WO 1999-FR703 W 19990326

AB The invention concerns the use of at least an **enterobacteria outer membrane protein A** fragment or a Klebsiella membrane protein (P40) fragment for prepg. a pharmaceutical compn. for nasal delivery, to improve a mammal's immunity to an antigen or a hapten.

L25 ANSWER 23 OF 30 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-583089 [50] WPIDS
CROSS REFERENCE: 2001-358083 [38]
DOC. NO. CPI: C1999-169768
TITLE: Immunogenic composition containing bacterial outer membranr protein conjugated or fused to antigen or hapten, for nasal administration, to protect against respiratory pathogens.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): ANDREONI, C; **BAUSSANT, T**; HAEUW, J; NGUYEN, T; RAULY, I; N'GUYEN, T; HAEUW, J F; NGUYEN, T N
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
FR 2776521	A1	19991001	(199950)*		64
WO 9949892	A2	19991007	(199950)	FR	
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CN JP MX US					
AU 9929391	A	19991018	(200010)		
BR 9909180	A	20001205	(200101)		
EP 1066054	A2	20010110	(200103)	FR	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1301176	A	20010627	(200158)		
MX 2000009490	A1	20010301	(200170)		
JP 2002509897	W	20020402	(200225)		55

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2776521	A1	FR 1998-3814	19980327
WO 9949892	A2	WO 1999-FR703	19990326
AU 9929391	A	AU 1999-29391	19990326
BR 9909180	A	BR 1999-9180	19990326
		WO 1999-FR703	19990326
EP 1066054	A2	EP 1999-910434	19990326
		WO 1999-FR703	19990326
CN 1301176	A	CN 1999-806265	19990326
MX 2000009490	A1	MX 2000-9490	20000927
JP 2002509897	W	WO 1999-FR703	19990326
		JP 2000-540854	19990326

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9929391	A	Based on	WO 9949892
BR 9909180	A	Based on	WO 9949892
EP 1066054	A2	Based on	WO 9949892
JP 2002509897	W	Based on	WO 9949892

PRIORITY APPLN. INFO: FR 1998-3814 19980327
AN 1999-583089 [50] WPIDS
CR 2001-358083 [38]
AB FR 2776521 A UPAB: 20020418
NOVELTY - Use of at least one fragment (I) of a bacterial membrane protein in a composition for nasal administration to improve immunity, in mammals, against an antigen or hapten (II) is new.

DETAILED DESCRIPTION - (I) is derived from:

(1) the outer membrane protein (Omp) A of an **enterobacterium**, or

(2) a Klebsiella membrane protein.

ACTIVITY - Antiviral; antibacterial.

MECHANISM OF ACTION - Induction of specific immune response.

USE - (I) and (II) conjugates, or fusion proteins (or host cells expressing the fusions), are particularly used in vaccines to immunize against viruses and bacteria that cause respiratory infections, specifically respiratory syncytial virus (RSV) in humans or cattle.

ADVANTAGE - The use of (I), from a species other than that from which (II) is derived, induces a protective response against (II), even without an adjuvant, since most adults will already be sensitized against (I), although the (I)-(II) product will induce an anti-(II) response even in subjects who are not pre-sensitized. Mice, some sensitized to the **Klebsiella pneumoniae** strain I145, were immunized intranasally with a conjugate of the synthetic respiratory syncytial virus (RSV) peptide G1' (O = ornithine) NSIDSNNPTOWAISKCC with the recombinant **K. pneumoniae outer membrane protein A**, P40, at a dose of 10 mu g peptide. Two more doses were given at 10 day intervals. A G1'-specific response, both immunoglobulin (Ig) G and IgA, was induced in sensitized animals after one injection and in naive animals after two injections. In all cases the response was strengthened by the third injection. The IgG response was a mixture of Th1 and Th2 types. Dwg.0/10

L25 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 19
ACCESSION NUMBER: 1999:709825 HCAPLUS
DOCUMENT NUMBER: 132:34413
TITLE: Carrier properties of a protein derived from **outer membrane protein A** of **Klebsiella pneumoniae**
AUTHOR(S): Rauly, Isabelle; Goetsch, Liliane; Haeuw, Jean-Francois; Tardieux, Christine; **Baussant, Thierry; Bonnefoy, Jean-Yves**; Corvaia, Nathalie
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint Julien en Genevois, Fr.
SOURCE: Infection and Immunity (1999), 67(11), 5547-5551
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have recently cloned a new protein, recombinant P40 (rP40). When tested in vivo after conjugation to a B-cell epitope, rP40 induces an important antibody response without the need for adjuvant. To characterize its potency, this carrier protein was coupled to a peptide derived from respiratory syncytial virus attachment G protein (G1'). After immunization of mice with the rP40-G1' conjugate, strong antipeptide antibodies were detected, whereas peptide alone was not immunogenic. To emphasize the carrier properties of rP40, a polysaccharide derived from Haemophilus influenzae type b (Hib) was coupled to it. IgG responses against the Hib polysaccharide were obsd. after coupling to rP40. Interestingly, an antipeptide antibody response was obsd. despite preexisting anti-rP40 antibodies generated by preimmunization with rP40. In addn., rP40 compares well with the ref. carrier protein, tetanus toxoid (TT), since antibody responses of equal intensity were obsd. when a peptide or a polysaccharide was coupled to TT and rP40. Moreover, rP40 had advantages compared to TT; e.g., it induced a mixed Th1/Th2 response, whereas TT induced only a Th2 profile. Together, the results indicate that rP40 is a novel carrier protein with potential for use as an alternative carrier for human vaccination.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 20
ACCESSION NUMBER: 1998:212045 HCAPLUS
DOCUMENT NUMBER: 128:320500
TITLE: IgE versus IgG4 production can be differentially regulated by IL-10
AUTHOR(S): **Jeannin, Pascale; Lecoanet, Sybille**; Delneste, Yves; Gauchat, Jean-Francois; Bonnefoy, Jean-Yves
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint-Julien en Genevois, F-74164, Fr.
SOURCE: Journal of Immunology (1998), 160(7), 3555-3561
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Allergen-specific IgE plays a key role in the physiopathol. of allergic disorders. This IgE response is usually accompanied by a prodn. of IgG4. Indirect evidence suggests that IgG4 may not be a sensitizing Ab but, in contrast, could be protective. As such, it may be of potential therapeutic interest to selectively modulate IgE vs. IgG4 prodn. To date, IgE and IgG4 switching seems to be controlled by common mechanisms. The authors report here that IL-10 has a different effect on IgE vs. IgG4 prodn. by PBMC. IL-10 decreases .epsilon. transcript expression and IgE prodn. induced by IL-4 when added during the first 3 days of in vitro culture, suggesting that IL-10 decreases IL-4-induced IgE switching. In contrast, if added later on B cells that are already IgE switched, IL-10 potentiates IgE prodn. Interestingly, whatever the time of addn., IL-10 augments IL-4-induced .gamma.4 transcript expression and IgG4 prodn., with a maximal effect when added during the first 3 days. As IL-10 is not a switch factor for IgG4, it is likely that

IL-10 enhances IgG4 prodn. by potentiating IL-4-induced IgG4 switching. However, IL-10 may also act by enhancing the growth and/or differentiation of cells that are already IgG4 committed. Finally, CD40 ligation reverses the early down-regulating effect of IL-10 on IgE prodn. These results are the first evidence of a mol. that differentially regulates IgE vs. IgG4 prodn., thereby suggesting the existence of a pathway(s) selectively controlling their prodn.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 21
ACCESSION NUMBER: 1998:487391 HCAPLUS
DOCUMENT NUMBER: 129:215413
TITLE: The recombinant **Klebsiella pneumoniae** outer membrane protein **OmpA** has carrier properties for conjugated antigenic peptides
AUTHOR(S): Haeuw, Jean-Francois; Rauly, Isabelle; Zanna, Laurence; Libon, Christine; Andreoni, Christine; Nguyen, Thien Ngoc; **Baussant, Thierry**; **Bonnefoy, Jean-Yves**; Beck, Alain
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, Saint Julien en Genevois, F-74164, Fr.
SOURCE: European Journal of Biochemistry (1998), 255(2), 446-454
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Klebsiella pneumoniae OmpA**, the 40-kDa major protein of the outer membrane, was cloned and expressed in Escherichia coli. The recombinant protein was produced intracellularly in E. coli as inclusion bodies. Fusion of a short peptide to the N-terminus of native P40 facilitated high-level expression of the recombinant protein. Purified recombinant P40 was analyzed to verify purity and structural integrity. The mol. mass of purified recombinant P40 detd. by electrospray mass spectrometry was 37,061 Da, in agreement with the theor. mass deduced from the DNA sequence. Specific proliferation of recombinant-P40-primed murine lymph node cells in response to recombinant P40 stimulation in vitro indicated the presence of a T-cell epitope on recombinant P40. The induction of high serum antibody titers to a synthetic peptide derived from the attachment protein G of the respiratory syncytial virus when chem. coupled to recombinant P40 indicated that the protein had potent carrier properties.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 27 OF 30 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:414077 BIOSIS
DOCUMENT NUMBER: PREV199800414077
TITLE: P40: A promising new carrier protein.
AUTHOR(S): Rauly, I.; Goetsch, L.; Libon, C.; Beck, A.; Heauw, J. F.; Guyen, T. N.; **Baussant, T.**;

Bonnefoy, J. Y.; Corvaia, N.
CORPORATE SOURCE: Centre d'Immunologie Pierre Fabre, 5 Av. Napoleon III. BP 497, F-74164 Saint Julien Genevois France
SOURCE: Research in Immunology, (Jan., 1998) Vol. 149, No. 1, pp. 99.
Meeting Info.: Euroconference on New Trends in Vaccine Research and Development: Adjuvants, Delivery Systems and Antigen Formulations Paris, France February 26-28, 1998
ISSN: 0923-2494.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 22
ACCESSION NUMBER: 1998:275804 HCAPLUS
DOCUMENT NUMBER: 129:63786
TITLE: Chromosomal sequencing using a PCR-based biotin-capture method allowed isolation of the complete gene for the **outer membrane protein A** of **Klebsiella pneumoniae**
AUTHOR(S): Nguyen, Thien Ngoc; Samuelson, Patrik; Sterky, Fredrik; Merle-Poitte, Christine; Robert, Alain; **Baussant, Thierry**; Haeuw, Jean-Francois; Uhlen, Mathias; Binz, Hans; Stahl, Stefan
CORPORATE SOURCE: Centre d'Immunol. Pierre Fabre, Saint-Julien en Genevois, F74 164, Fr.
SOURCE: Gene (1998), 210(1), 93-101
CODEN: GENED6; ISSN: 0378-1119
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By employing a novel biotin- and PCR-assisted capture method, which allows detn. of unknown sequences on chromosomal DNA, the gene for the **outer membrane protein A** (**OmpA**) of **Klebsiella pneumoniae** has been isolated and sequenced to completion. The method involves linear amplification of DNA from a biotinylated primer annealing to a region with known sequence. After capture of the amplified single-stranded DNA on to paramagnetic beads, unspecifically annealing primers, i.e. arbitrary primers, were used to generate fragments with only partly detd. nt sequences. The homol. of the sequenced gene to **ompAs** of related bacteria is discussed. The **ompA** gene was assembled for intracellular expression in Escherichia coli, and two different fusion proteins were produced and recovered with good yields. The importance of the novel chromosomal sequencing method for gene isolation in general and the potential use of the **OmpA** fusion proteins are discussed.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 29 OF 30 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:98968 BIOSIS
DOCUMENT NUMBER: PREV199799398171
TITLE: The 25kDa soluble CD23 interacts with CD11b-cD18 and CD11c-CD18 on human monocytes and activates type III

constitutive nitric oxide synthase.

AUTHOR(S): **Aubry, Jean-Pierre; Lecoanet, Sybille**; Dugas, Nathalie; Gauchat, Jean-Francois; Graber, Pierre; Dugas, Bernard; Bonnefoy, Jean-Yves

CORPORATE SOURCE: Geneva Biomed Research Inst., Glaxo Wellcome, Glaxo Switzerland

SOURCE: Tissue Antigens, (1996) Vol. 48, No. 4-2, pp. 423. Meeting Info.: 6th International Workshop and Conference on Human Leukocyte Differentiation Antigens Kobe, Japan November 10-14, 1996 ISSN: 0001-2815.

DOCUMENT TYPE: Conference; Abstract

LANGUAGE: English

L25 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:996645 HCAPLUS

DOCUMENT NUMBER: 124:200190

TITLE: Peptide fragments of respiratory syncytial virus G protein and vaccines containing same

INVENTOR(S): Binz, Hans; N'guyen, Ngoc Thien; **Baussant, Thierry**; Trudel, Michel

PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.

SOURCE: PCT Int. Appl., 90 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9527787	A1	19951019	WO 1995-FR444	19950406
W: AU, CA, JP, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2718452	A1	19951013	FR 1994-4009	19940406
FR 2718452	B1	19960628		
CA 2187083	AA	19951019	CA 1995-2187083	19950406
AU 9523109	A1	19951030	AU 1995-23109	19950406
AU 708856	B2	19990812		
EP 754231	A1	19970122	EP 1995-916721	19950406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09511404	T2	19971118	JP 1995-526123	19950406
NZ 329833	A	20000228	NZ 1995-329833	19950406
EP 1111053	A2	20010627	EP 2000-126606	19950406
EP 1111053	A3	20010808		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6113911	A	20000905	US 1996-721979	19961004
AU 9889554	A1	19990107	AU 1998-89554	19981027
AU 728139	B2	20010104		
US 6537556	B1	20030325	US 2000-582876	20000630
US 6410030	B1	20020625	US 2000-654289	20000901
US 2003064078	A1	20030403	US 2002-91257	20020305

PRIORITY APPLN. INFO.: FR 1994-4009 A 19940406
AU 1995-23109 A3 19950406

Searcher : Shears 308-4994

EP 1995-916721 A3 19950406
WO 1995-FR444 W 19950406
US 1996-721979 A1 19961004
US 2000-654289 A1 20000901

AB A polypeptide useful as an immunogen comprises all or fragments of residues 130-230 of the G protein of the human respiratory syncytial virus subgroups A and B, or of the bovine respiratory syncytial virus, or a sequence at least 80% homologous thereto. The immunogenic peptides/proteins may be conjugated to a carrier protein such as the **OmpA** protein, p40 of **Klebsiella pneumoniae**, or the human serum albumin receptor. A peptide fragment of respiratory syncytial virus subgroup A was coupled to recombinant p40 with glutaraldehyde. Mice immunized with this conjugate were completely protected from challenge with the virus.

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